

2018

RESEARCH ANNUAL REPORT



2018 RESEARCH ANNUAL REPORT

MILESTONES

INITIATIVES

INNOVATION

COLLABORATION

HONORS

VISIONARIES

DISCOVERY

INSPIRATION

FACTS & FIGURES

MILESTONES >

MILESTONES



- 4 PIONEERING MATERNAL-FETAL MEDICINE UNIT CELEBRATES 10 YEARS AND 3,600 DELIVERIES
- 5 FDA APPROVES FIRST DRUG FOR CHILDREN WITH RELAPSING MULTIPLE SCLEROSIS
- 6 DIVISION OF ALLERGY AND IMMUNOLOGY DESIGNATED A CENTER OF EXCELLENCE
- 7 POLICYLAB MARKS 10TH ANNIVERSARY BY SETTING GOALS FOR THE NEXT DECADE
- 8 NUMEROUS MILESTONES DRIVE CAR'S FIRST 10 YEARS
- 10 CPCE MARKS A DECADE OF ANSWERING 'WHAT WORKS IN HEALTHCARE



PIONEERING MATERNAL-FETAL MEDICINE UNIT CELEBRATES 10 YEARS AND 3,600 DELIVERIES

[The Garbose Family Special Delivery Unit](#), the world's first obstetrical care unit for healthy mothers carrying fetuses with known birth defects, marked its 10th anniversary this year. Children's Hospital of Philadelphia celebrated the milestone with a special ceremony honoring the unit, which is the delivery arm of CHOP's internationally recognized [Center for Fetal Diagnosis and Treatment \(CFDT\)](#).

Launched in 2008, the 13-bed unit fulfills an important need in maternal-fetal medicine by allowing mother and baby to be simultaneously cared for in one medical center by a highly specialized, multidisciplinary team. Over the past decade, it has seen more than 3,600 deliveries — an average of 450 to 500 deliveries a year — for patients from all 50 states and dozens of countries.

Lynne and Bill Garbose made the unit possible with their lead philanthropic gift, motivated by the loss of their own newborn infant 30 years ago due to a fatal heart defect. Their loss came at a time when parents were unable to deliver their critically ill babies at a pediatric hospital anywhere in the United States.

Today, the unit houses two operating rooms for cesarean deliveries and fetal surgery. Its multidisciplinary team includes experts in maternal-fetal medicine, reproductive genetics, obstetrics, surgery, anesthesiology, neonatology, fetal cardiology, genetic counseling, midwifery, fetal imaging, social work, palliative care, lactation consulting, and respiratory therapy. In addition, fetal therapy coordinators guide patients through their experience.

What will the next 10 years bring? The Garboses decided to fund a new Garbose Family Endowed Research Fellowship in Pediatric and Fetal Surgery in a specialized laboratory program within the CFDT. The fellowship will support fetal researchers working to generate new breakthroughs and establish a pipeline of physician-researchers to help lead the next generation of fetal medicine experts.



FDA APPROVES FIRST DRUG FOR CHILDREN WITH RELAPSING MULTIPLE SCLEROSIS

The Food and Drug Administration approved the first disease-modifying drug for children and adolescents with relapsing forms of multiple sclerosis (MS). [Brenda Banwell, MD](#), Chief of the Division of Neurology at Children's Hospital of Philadelphia, served as co-principal investigator of the study that supported the pediatric approval.

The drug, fingolimod, has been proven to significantly reduce relapses and brain lesions in children as young as 10 years old. It was previously indicated only for adult patients 18 or older to help control MS relapses, brain lesions, and disability progression. The expanded approval is expected to bring new hope for younger MS patients.

"Repeated relapses are more common in young people with MS than in adults," Dr. Banwell noted. "This is heartening news for patients and their families."

The FDA named fingolimod, which is marketed in the United States and Europe by Novartis, a breakthrough therapy in late 2017 for children with relapsing MS. Early study results found that fingolimod could reduce the frequency of MS flare-ups in pediatric patients by nearly 82 percent compared to other drug treatments. Later study findings indicated fingolimod reduced pediatric patients' relapse rate and development of new brain lesions, and it slowed disability progression.

A microscopic image showing various cells and tissue structures. In the foreground, there are red, textured structures resembling blood vessels or skin cells. Above them, several blue, star-shaped cells with long, thin projections are visible against a dark background.

DIVISION OF ALLERGY AND IMMUNOLOGY DESIGNATED A CENTER OF EXCELLENCE

The World Allergy Organization (WAO) named the Division of Allergy and Immunology at Children’s Hospital of Philadelphia a Center of Excellence. The mission of the WAO’s Centers of Excellence is to intensify and accelerate multidisciplinary scientific and clinical innovation, education, and advocacy worldwide in allergy, asthma, and clinical immunology. The WAO also designated the Section of Allergy and Immunology at the Hospital of the University of Pennsylvania a Center of Excellence.

“We are honored to be named as a WAO Center of Excellence,” said [Jonathan Spergel, MD, PhD](#), Section Chief of Allergy in the Division of Allergy and Immunology at CHOP. “This distinction recognizes not only the groundbreaking research being done at CHOP and Penn, but also the outstanding clinical care we deliver.”

CHOP’s Division of Allergy and Immunology is one of the largest pediatric allergy groups in the region and cares for patients with all aspects of allergic and immunologic issues. Its faculty has helped formulate many of the national guidelines used by physicians across the country and around the world. The division treats patients with difficult-to-control allergic disorders, including asthma and anaphylaxis. It also provides evaluation and drug desensitization for patients who have a history of anaphylactic reactions to necessary, life-saving medications.

Ongoing research efforts in collaboration with colleagues at CHOP and other institutions around the world are focused on eosinophilic esophagitis, allergen-specific immunoglobulin E (IgE)-mediated food allergies, food desensitization, asthma, and atopic dermatitis.



POLICYLAB MARKS 10TH ANNIVERSARY BY SETTING GOALS FOR THE NEXT DECADE

[PolicyLab](#) celebrated 10 years as a Center of Emphasis at Children's Hospital of Philadelphia Research Institute. To plan for the next 10 years, PolicyLab announced it is refining its focus and reorganizing its resources to benefit families, colleagues, and policymakers.

Founded in 2008, PolicyLab researches, develops and implements evidence-based solutions in response to community needs and child health policy priorities. Researchers collaborate with communications and policy professionals to translate their work for program and policy audiences.

PolicyLab faculty and staff identified four areas, or portfolios, of child and family health to target in the next decade: Healthcare Coverage, Access and Quality; Intergenerational Family Services; Health Equity; and Adolescent Health and Well-being. Comprehensive goals have been developed by PolicyLab for each of the four areas.

In the Healthcare Coverage, Access and Quality portfolio, interdisciplinary teams will focus on aligning health insurance coverage, clinical services, and community service organizations with children's unique needs to improve children's health and well-being.

The Intergenerational Family Services portfolio will address the increasing barriers that pediatric patients' parents and caregivers face in maintaining their own health and well-being, which is essential to keeping families healthy, by building support for sustainable family-centered programs in pediatric settings.

In the Health Equity portfolio, researchers will evaluate programs and policies to ensure that they do not inadvertently create avoidable or remediable differences in outcomes for marginalized children and adolescents. Challenges faced by racial/ethnic minorities, immigrants and refugees, LGBTQ youth, youth with complex medical needs, and those in the child welfare and juvenile justice systems, will be addressed.

The Adolescent Health and Well-being portfolio will focus on helping parents understand the challenges that adolescents with unique needs face in transitioning to healthy, productive adults. PolicyLab also aims to influence programs and policies addressing teens' reproductive and sexual health, mental health, and special healthcare needs.



NUMEROUS MILESTONES DRIVE CAR'S FIRST 10 YEARS

As a spectrum disorder, autism spectrum disorder (ASD) can look very different from one person to the next, with hundreds of possible genetic mutations that seem to play a role in how ASD is expressed in each individual. Gathering data and funding studies of the size and scope necessary to account for autism's myriad expressions has been out of reach — until now. Established in October 2008, the [Center for Autism Research](#) (CAR) is uniquely poised to lead autism research into a new era.

Over the last decade, CAR has sought to understand the causes of ASD in order to develop effective treatments through research; to serve the needs of individuals with ASD and their families through education and guidance throughout the lifespan; and to train the next generation of master clinicians and scientists in state-of-the-science best practices for autism screening, diagnosis, and treatment.

“CHOP offers a unique set of circumstances that makes it possible to surmount these persistent challenges in autism research,” said [Robert T. Schultz, PhD](#), CAR's scientific director. “CHOP's vast patient base of 10,000 patients per year with ASD combined with unparalleled clinical and research expertise in multiple specialties affords us an extremely rare opportunity to conduct research that is rigorous, reproducible, and ultimately translatable: to accelerate the pace at which we're able to improve care and long-term outcomes for patients with ASD within the CHOP Care Network and throughout the country.”

A collaborative effort between [Children's Hospital of Philadelphia](#) and the [University of Pennsylvania](#), CAR and its researchers have achieved numerous milestones over the past 10 years.

Time magazine named the [discovery of autism gene variants](#) by [Hakon Hakonarson, MD, PhD](#), director of the Center for Applied Genomics at CHOP, a top 10 medical breakthrough for 2009. “[To that point], researchers knew little about the genetic component of ASD; and what they did know was related to syndromic, rare forms of ASD seen in other conditions, such as Fragile X syndrome, 22q11.2 Deletion and Duplication Syndromes, and Prader-Willi syndrome,” Dr. Hakonarson stated.

The following year, [Timothy Roberts, PhD](#), vice-chair of research for the Department of Radiology at CHOP, discovered that children with ASD process sounds a fraction of a second slower than typically developing peers, leading to cascading delays.

The 2011 Infant Brain Imaging Study found the brains of infants who develop ASD follow different developmental trajectory from 6 months of age, affecting brain connections later in life. In 2017, a [significant follow-up finding](#) revealed differences in brain activity patterns at 6 months old can predict which children will develop autism at age 2. A Center of Emphasis at CHOP, CAR established the Technology and Innovation Lab in 2015, which focuses on developing new technologies to revolutionize autism diagnosis and treatment. Two years later, the lab created a tool to help diagnose autism based on a three-minute video of social conversation.

In 2016, [John Herrington, PhD](#), assistant professor in the Department of Child Psychiatry and Behavioral Science at the Perelman School of Medicine, found the amygdala to be smaller and more active in children who have ASD as well as an anxiety disorder. These findings suggest that symptoms of anxiety aren't merely a facet of the core ASD symptoms but suggest anxiety can co-occur as a separate diagnosis in children with ASD.

And this year, CAR undertook the first longitudinal examination of the effectiveness of universal screening of autism using the Modified Checklist for Autism in Toddlers (M-CHAT). Looking to the future, CAR is building an integrated clinical/research program known as the "Autism Learning Health System" that is a testing ground for new treatments and models of care, with the support of patients and families, research collaborators, and partners like the Philadelphia Eagles. Learn more about this groundbreaking development in [CAR's 10th Anniversary Report](#).



CPCE MARKS A DECADE OF ANSWERING WHAT WORKS IN HEALTHCARE

Celebrating its 10-year anniversary, the [Center for Pediatric Clinical Effectiveness](#) (CPCE) continues to discover and share knowledge about best practices in pediatric care. The Center of Emphasis at [Children's Hospital of Philadelphia Research Institute](#) achieves this goal by facilitating, organizing, and centralizing the performance of clinical effectiveness research. Put simply, it looks for “what works?” in healthcare.

Among its many highlights from the past decade, CPCE promotes antibiotic stewardship by providing achievable benchmarks and high-impact targets for improving antibiotic prescribing, then developing and implementing effective interventions. For example, CPCE's [Promoting Antibiotic Stewardship in Pediatric Outpatient Settings](#) summarizes seven years of research to improve the effectiveness and acceptability of outpatient antimicrobial stewardship. The research brief notes that antimicrobial stewardship programs can improve the patient experience, reduce costs for payers, and lead to healthier populations through reduction of antibiotic overuse and resistance.

The puzzling growing incidence of pediatric kidney stones has become another area of emphasis for CPCE. With uncertainty of how to best evaluate children with suspected kidney stones and effectively decrease recurrence for patients whose first stone developed during childhood, CPCE seeks to address these knowledge gaps. Research includes studies on the role of temperature and antibiotics in kidney stone risk and mobile device hydration reminders for adolescents. CPCE also strives to close the knowledge gap in pediatric HIV prevention and treatment research, as data for best practices center on adult cases. In particular, researchers are addressing challenges with treatment adherence unique among adolescents with HIV, as well as increasing the information needed to make pediatric formulations of newer HIV medications available and to understand which medicines work best in this population.

Understanding the pros and cons of physiologic monitoring — in both clinical settings and at home — has drawn CPCE's attention as well. When healthcare workers experience alarm fatigue, they become overwhelmed, distracted by, or desensitized to the numbers of alarms that monitors activate, which can lead to delayed response times or missed alarms. A CHOP-led team used a video-based approach to gather data on staff response times and false alarm rates. In another study, the same CHOP researcher found at-home infant physiological monitors may cause undue alarm to parents, with no evidence of medical benefits, especially to healthy babies.



INITIATIVES

- 12 NEW CAMPAIGN LAUNCHED TO RAISE \$1 BILLION
- 13 TWO PIONEERING PROGRAMS ACHIEVE PRESTIGIOUS FRONTIER STATUS
- 14 ARCUS PEDIATRIC KNOWLEDGE NETWORK BUILDS FOUNDATION FOR SOPHISTICATED DATA INTEGRATION
- 15 NEW CENTER FOR COMPUTATIONAL AND GENOMIC MEDICINE LAUNCHES
- 16 OFFICE OF ACADEMIC TRAINING AND OUTREACH PROGRAMS SUPPORT RESEARCH COMMUNITY



NEW CAMPAIGN LAUNCHED TO RAISE \$1 BILLION

Children's Hospital of Philadelphia has launched the most ambitious fundraising effort in its 162-year history, with the goal of raising a record-setting \$1 billion by 2020.

The campaign, "For Tomorrow's Breakthroughs: The Campaign for Children's Hospital of Philadelphia" will fund the development of comprehensive, wide-ranging advances to save more children's lives. It's off to a great start — the campaign has already reached the \$800 million mark.

Donations will support five critical areas. Funds will go toward research to support the development of new treatments for the most complex conditions in order to set the standard for pediatric healthcare worldwide. Creating an exceptional patient-family experience by providing the most advanced treatments at the best facilities, with the most comprehensive support programs, will also be a funding priority.

Focusing on training pediatric care leaders of the future, including healthcare providers, specialists, and researchers, will give staff opportunities to advance their education so they can offer the best care possible for children and families. Funds raised will further support outreach to children and families in need in order to improve the health and well-being of children and families in the region, nation, and world.

Finally, the increased funding will give CHOP the resources to act quickly on new opportunities and meet unexpected needs. The Children's Fund provides financial resources to take a broad range of actions that can make a difference, such as purchasing revolutionary new equipment, moving a promising discovery forward, or hiring a leading expert.



TWO PIONEERING PROGRAMS ACHIEVE PRESTIGIOUS FRONTIER STATUS

Children's Hospital of Philadelphia awarded two centers Frontier Program status in 2018, providing the Immune Dysregulation and Food Allergy Programs with the support and resources needed to drive world-changing discoveries, deliver life-saving therapies, and strengthen the bridge between research breakthroughs and exemplary clinical care.

UNRAVELING THE ARCHITECTURE OF IMMUNE SYSTEM DISORDERS

With a team of clinical and scientific leaders across multiple disciplines, the Immune Dysregulation Program will enable the diagnoses of patients with rare, complex diseases of the immune system and develop novel precision drugs for treatment.

"If we can discover a mutation in a patient's gene, then understand why and how that mutation causes a problem with the immune system, we can think of a medicine that can attack that particular problem," said [Edward Behrens, MD](#), chief of the Division of Rheumatology and co-leader of the Immune Dysregulation Program alongside [Kathleen Sullivan, MD](#), PhD; [Michele Lambert, MD, MSTR](#); and [David Teachey, MD](#).

In 2015, Dr. Behrens and his team [diagnosed a patient with an autoinflammatory disease caused by a mutation of the NLRC-4 protein](#) and successfully developed exactly that type of precision treatment approach. According to Dr. Behrens, Frontier support empowers him and fellow scientists to conduct the same in-depth investigation for even more patients, armed with resources they have dreamed of obtaining for years. These include novel laboratory testing, rapid genetic testing, and an expanded multidisciplinary clinical staff.

ADDRESSING THE UNKNOWNNS IN FOOD ALLERGY RESEARCH

The [Food Allergy Center](#) at CHOP, already a nationally recognized program for its expertise in all four types of food allergy, will utilize Frontier support to raise their clinical care standards by developing new diagnostic assays and testing novel therapies.

"The Frontier Program allows us to really bring new clinical and research endeavors to patients," said [Jonathan Spergel, MD, PhD](#), chief of the Allergy Section at CHOP and co-director of the Food Allergy Frontier Program alongside co-directors [Terri Brown-Whitehorn, MD](#), and [Megan O. Lewis, MSN, CRNP](#). "There are so many important unanswered questions needed to improve care, and we will begin to answer those questions and move things forward to the ultimate goal: Treat, prevent, and cure food allergies."

In partnership with Oxford University researchers, Dr. Spergel and his team are currently studying how to predict which patients will develop a severe reaction to a food allergen versus a mild one. By looking at cell function on a genome-wide array before and after a food challenge, Dr. Spergel hopes to elucidate not just who is at risk for a severe reaction, but what is different at the cellular level when such a reaction occurs.

The program also has a robust research pipeline for [eosinophilic esophagitis \(EoE\)](#), an inflammatory disease of the esophagus triggered by food allergens. Dr. Spergel's previous research showed that [T-cells become activated in response to milk allergens in patients with EoE](#), and the next step involves studying T-cell response to other foods and developing a clinically useful test to measure what foods might be causing EoE.



Aptly named Arcus, which means “arch” in Latin, the new platform will give investigators across campus access to a robust data platform that bridges the wealth of clinical and research data at Children’s Hospital of Philadelphia.

With about 2.6 million patients on record at CHOP, Arcus is an ambitious project that uses a library science approach to catalog, cross reference, and enrich the data produced over the course of patients' clinical encounters and research study visits throughout childhood and adolescence. Hundreds of terabytes of data — from MRIs, CTs, bedside monitors, laboratory results and more — have been collected through CHOP's single electronic medical record since about 2010. In addition, the Research Institute currently has about six petabytes of research data, mainly genomic and molecular biology data.

Arcus will link the vast quantities of pediatric data CHOP generates as a clinical enterprise with the data it generates as a research enterprise to produce a more holistic picture of pediatric health and disease. Importantly, the Arcus team also includes patient families who represent the patient perspective in the development of such a significant new data resource.

A growing cohort of pilot studies conducted by scientists who are investigating a wide range of scientific questions along the research continuum are driving this one-of-its-kind data library. As data sets are continually added, Arcus will become a powerful key to unlocking chronic and complex pediatric diseases and opening new viewpoints into how healthy children grow and develop.



NEW CENTER FOR COMPUTATIONAL AND GENOMIC MEDICINE LAUNCHES

A new Center for Computational and Genomic Medicine at Children's Hospital of Philadelphia will drive biological discoveries and medical innovations by leveraging recent advancements in sequencing technology and computational biology. The Center will contribute to CHOP's entire ecosystem of research, including collaborations with the Center for Cellular and Molecular Therapeutics and the Department of Biomedical and Health Informatics, among others.

[Yi Xing, PhD](#), moved his lab and team of about 20 investigators from University of California Los Angeles to CHOP's research campus and officially opened the Center Sept. 1. It will provide an intellectual home for recruiting tenure track faculty who are not only adept at using existing technology, but also can develop new genomic technologies or computational tools that can be offered to a broader community of scientists. The Center will have a hybrid character — computational biology research will pave the way for new projects in wet laboratories.

"Our goal is to make the center an engine for technological and biomedical innovation," said Dr. Xing, who also is a professor of Pathology and Laboratory Medicine in the [Perelman School of Medicine](#) at the [University of Pennsylvania](#). "There will be tight interaction from both the basic science and technology side, as well as the translational and clinical side of genomics and computational biology."

Dr. Xing and his team have addressed stimulating concepts in the field, such as defining the fundamental data structure and algorithms for looking at the complexity of RNA. Because so many human mutations disrupt RNA and contribute to disease, Dr. Xing's work in mastering how to manage and interpret big data offers opportunities for improved diagnoses and treatments.

"A fun part about working in the area of genomics and computational biology is the technologies are constantly changing, and they generate a lot of interesting problems to solve," Dr. Xing said. "In turn, those technologies generate a huge amount of data. A big part of our lab is to develop innovative computational methods for integrating those larger scale data sets in order to translate big data into knowledge."

Dr. Xing holds the new Francis West Lewis Chair in Computational and Genomic Medicine at CHOP.



**OFFICE OF ACADEMIC TRAINING AND OUTREACH
PROGRAMS SUPPORT RESEARCH COMMUNITY**

We are always striving for excellence at Children’s Hospital of Philadelphia Research Institute — from our first days of orientation to when we become leaders and mentors at the top of our fields. A new [Office of Academic Training and Outreach Programs \(ATOP\)](#) launched in 2018 to create engaging and comprehensive educational experiences for researchers and their staffs at all levels of the career ladder.

The new office led by Wendy Reed Williams, PhD, senior director, reflects three tiers of service: academic training, outreach programs, and specialty programs and diversity. The academic training arm of the office includes expanded and formalized support with an emphasis on academic success skill training programs, in partnership with key faculty across the Research Institute. Outreach programs creates internships, events, and career exposure opportunities for students and community partners to develop future generations of leaders in child health. The newest service tier focuses on developing targeted research programs and pilot grant opportunities, while also building and supporting a diverse workforce at the Research Institute.

ATOP will add and expand upon its core services for research staff and trainees to meet the educational needs of the research community while promoting a culture of best practices and integrity in research. Some of the initiatives that will be rolled out over the course of FY2019 and beyond include reaching a wider audience of early career researchers, offering new research opportunities for science-minded undergrads and high school students, developing a formalized diversity support infrastructure at the Research Institute, and creating discipline-specific research programs and pilot grant opportunities for scientists-in-training, among others.

This transition and expansion of this critical support office will be conducted under the purview of Chief Scientific Strategy Officer, Beverly Davidson, PhD, to align its work with key strategic initiatives at the Research Institute.

INNOVATION



- 18 IMPACT OF INNOVATION
- 21 CHOP TO ADDRESS KEY CHALLENGES IN PEDIATRIC CLINICAL TRIALS
- 22 CHOP-LED PROJECT TO EASE BURDEN OF YOUNG ADULTS WITH SICKLE CELL DISEASE
- 23 RESEARCHERS ENLIST VISUAL EYE-TRACKING ALGORITHM TO ENHANCE CONCUSSION DIAGNOSIS
- 24 NOVEL APPROACHES CREATE HEALTHIER FUTURES FOR PATIENTS LIVING WITH INHERITED BLOOD DISORDERS

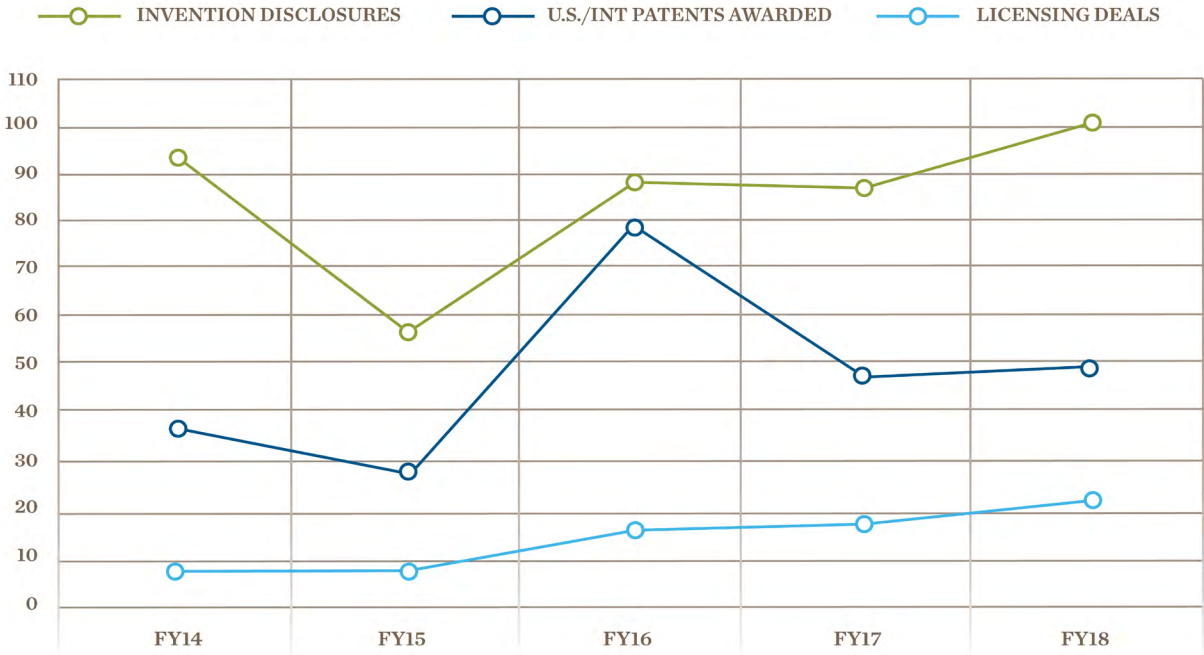


IMPACT OF INNOVATION

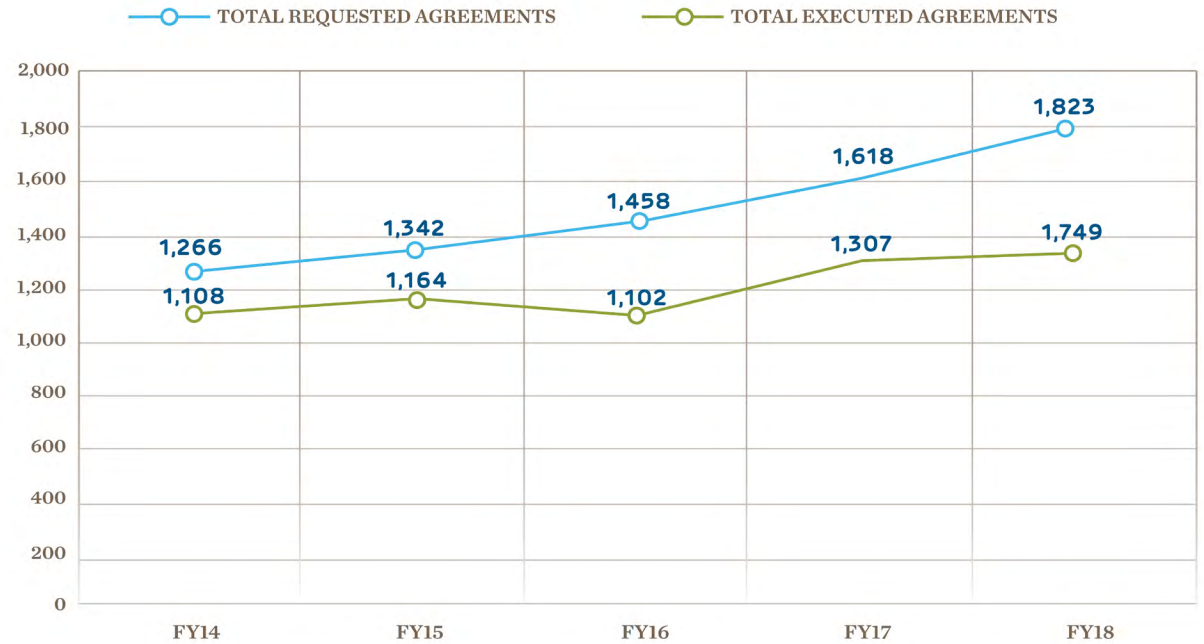
OFFICE OF TECHNOLOGY TRANSFER	FY 2017	FY 2018
Licensing Deals	15	20
Invention Disclosures Received from Inventors	87	101
U.S. Patent Applications Filed (Provisional)	29	36
U.S. Patent Applications Filed (Utility and Nationalized PCT)	29	25
U.S. Patents Awarded to CHOP	6	16
International Patent Applications Filed (PCT and Foreign)	62	136
International Patents Awarded to CHOP	41	33

OFFICE OF COLLABORATIVE AND CORPORATE RESEARCH CONTRACTS	FY 2017	FY 2018
Material Transfer Agreements (MTAs)	488	445
Confidential Disclosure Agreements (CDAs)	288	297
Data Use & Data Transfer Agreements (DUAs & DTAs)	186	250
Consulting Agreements	142	154
Other Agreements	203	203
TOTAL AGREEMENTS FULLY EXECUTED	1307	1349

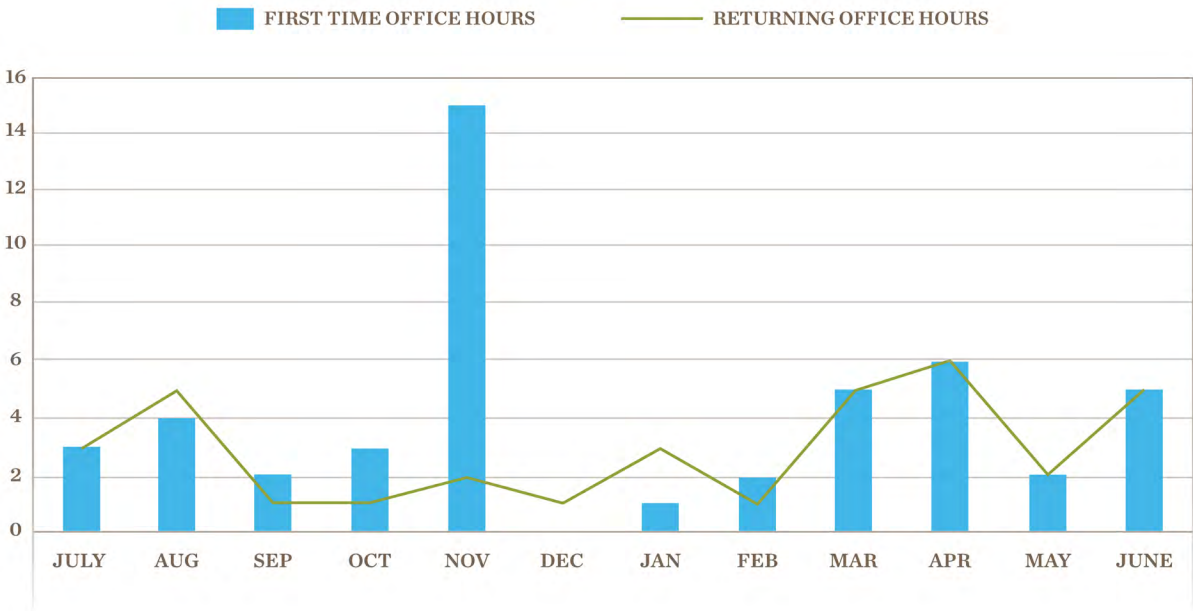
OFFICE OF TECHNOLOGY TRANSFER LICENSING & INTELLECTUAL PROPERTY



OFFICE OF COLLABORATIVE AND CORPORATE RESEARCH CONTRACTS



OFFICE OF ENTREPUENEURSHIP AND INNOVATION
FY 2018 OFFICE HOURS





CHOP TO ADDRESS KEY CHALLENGES IN PEDIATRIC CLINICAL TRIALS

Nearly 60 percent of drugs used in children and 90 percent of those used in neonates are prescribed off-label, said [Christopher Forrest, MD, PhD](#), a pediatrician at [Children's Hospital of Philadelphia](#). In addition, the lag from initial approval and labeling of a drug for adults and pediatric labeling stretches to nine years, a statistic that hasn't changed over the last decade.

"A lack of an integrated, efficient pediatric clinical trials infrastructure, misalignment of stakeholder interests, and studies that are poorly designed and not feasible are all contributing barriers to trials for new drugs and devices for children," Dr. Forrest said.

Change will be coming, though. CHOP serves as the coordinating center for [PEDSnet](#), a national network that conducts observational pediatric research, said Dr. Forrest, PEDSnet principal investigator.

PEDSnet is allied with the [Institute for Advanced Clinical Trials for Children](#) (I-ACT for Children), an independent nonprofit organization that works to improve the planning and completion of pediatric clinical trials. In October 2017, the Food and Drug Administration awarded a \$1 million cooperative agreement to I-ACT and its partners with the potential for \$1 million annually for an additional four years to meet this goal.

"This is an excellent opportunity for PEDSnet because it allows us to expand from observational to prospective trials," said Dr. Forrest of the funding.

Comprised of the nation's leading children's research hospitals, PEDSnet has established a novel real-world database of more than 6.5 million children's electronic health record data that can be used for feasibility assessments, cohort discovery, natural history, and observational studies, he said.

"Our primary focus in trials is to establish real-world effectiveness of diverse healthcare interventions," Dr. Forrest said. "PEDSnet will use these assets as it serves as the data and learning core for the Global Pediatric Clinical Trials Network, which aims to bring the kind of transformation necessary to engage diverse public and private stakeholders, re-engineer the current system, and catalyze existing expertise and resources."



CHOP-LED PROJECT TO EASE BURDEN OF YOUNG ADULTS WITH SICKLE CELL DISEASE

With a massive grant of nearly \$8.5 million, researchers at Children’s Hospital of Philadelphia’s Comprehensive Sickle Cell Center, PolicyLab, and Northwell Health’s Cohen Children’s Medical Center will help smooth a traditionally difficult point in the lives of adolescents and young adults with sickle cell disease.

“This is an incredibly impactful grant, and I’m proud to be working on this,” said [David Rubin, MD, MSCE](#), an attending physician and the founding co-director of [PolicyLab](#) at CHOP, who is one of two lead principal investigators of the project. “Youth with sickle cell disease have historically struggled in their transition to an adult world of medicine that’s often unprepared or unwilling to provide the care that they need.”

[Kim Smith-Whitley, MD](#), clinical director of the Division of Hematology and director of the [Comprehensive Sickle Cell Center](#) at CHOP, also is a co-principal investigator. Young adults with sickle cell disease experience increased rates of death during the transition from pediatric to adult care, and they use more healthcare services than all other age groups, she said. Community health worker programs and mobile health applications could help this patient population, but it’s unknown to what extent these interventions actually improve their lives.

In “Community Health Workers and Mobile Health for Emerging Adults Transitioning Sickle Cell Disease Care” (COMETS Trial), funded by the [Patient-Centered Outcomes Research Institute](#), researchers will compare the effectiveness of these two self-management support interventions vs. enhanced usual care to improve health-related quality of life and acute care use for transitioning youth with sickle cell disease, as well as identify and quantify mediators and moderators of intervention treatment effects. The COMETS Trial began recruiting patients in October 2018.

“The pressure to self-manage a chronic illness like this has never been greater,” Dr. Rubin said. “Being able to work among our partner sites to help achieve a successful transition for these youth — and build capacity for the youth who will come behind them — is a tremendous and humbling honor. If this work helps solidify the strategies not only in our backyard but serves as a template for other places in the country, all the better.”



RESEARCHERS ENLIST VISUAL EYE-TRACKING ALGORITHM TO ENHANCE CONCUSSION DIAGNOSIS

Clinician-scientists at Children’s Hospital of Philadelphia lead pioneering research evaluating the impact of advanced eye-tracking tools to detect deficits in children and adolescents with concussions. By studying the utility of visio-vestibular exams (VVE) and automated eye-tracking assessments, our researchers work at the cutting-edge of developing objective and rapid tools for concussion diagnoses as well as for predicting recovery time. In 2018, these breakthroughs were recognized across the scientific community and the [mainstream media](#).

“Many concussed youths have vision deficits, but if you aren’t looking for them, you won’t find them. If you don’t find them, you can’t treat them,” said [Christina L Master, MD, FAAP, CAQSM](#), co-lead of the Minds Matter program and primary care sports medicine specialist at CHOP. “Having reliable practical clinical tools that can detect vision deficits soon after a concussion injury is critical to improving concussion care for kids.”

In a study published in the [Clinical Journal of Sport Medicine](#), Dr. Master and colleagues found that 88 percent of 432 children in a concussion program presented with visio-vestibular deficits, such as problems with balance and tracking a moving object, that predicted prolonged concussion recovery. Furthermore, a team of CHOP researchers found that [the VVE was a feasible tool for clinicians in high-volume, acute care settings](#) and that the exam could help clinicians more accurately identify concussed patients.

Researchers in our [Center for Injury Research and Prevention](#), in collaboration with other institutions, also found that [an automated eye-tracking assessment](#) proved to be a successful objective and noninvasive method for identifying concussion. As an alternative to more subjective and symptom-based assessments, tracking a patient’s binocular eye movements while watching a video are what Dr. Master calls “one tool” in a clinician’s diagnostic toolbox.

After a head injury, either of these innovative tests could establish an earlier diagnosis and thus help families, clinicians, and teachers develop the appropriate accommodations during recovery.

Learn more about the use of [eye-tracking technology in concussion care](#).



NOVEL APPROACHES CREATE HEALTHIER FUTURES FOR PATIENTS LIVING WITH INHERITED BLOOD DISORDERS

Mitochondria, the power plants of a cell, generate the energy we need for nearly every organ or system in the body to function properly. [Shana McCormack, MD](#), an attending physician in the division of Endocrinology and Diabetes at CHOP and [assistant professor of Pediatrics](#) at Penn, along with colleagues at the University of Pennsylvania's Center for Magnetic Resonance and Optical Imaging, developed a noninvasive way to track mitochondria and gain insights into their bioenergetics.

The new approach is a unique magnetic resonance imaging tool, called [creatine chemical exchange saturation transfer](#) (CrCEST) MRI, that could help researchers study the impact of metabolic disease longitudinally in children. CrCEST detects changes in muscle creatine content before and after exercise. These changes allow researchers to estimate mitochondrial oxidative phosphorylation (OXPHOS) capacity, which is an important indicator of how the body generates energy.

In their study published in [JCI Insight](#), Dr. McCormack and her colleagues demonstrated that CrCEST was a viable technique for measuring OXPHOS capacity after exercise in individuals with [genetic mitochondrial disease](#), a group of conditions that can produce symptoms in many different organs, including fatigue, cardiac problems, diabetes, hearing and vision impairment, and more — depending on which cells within the body have disrupted mitochondria.

CrCEST has several benefits beyond the current techniques used to measure mitochondrial function, which often require a muscle biopsy. Along with being noninvasive, CrCEST gives researchers a high-resolution picture of mitochondrial function in different muscle groups simultaneously. With further development, the new tool may give physicians an objective biomarker to determine whether a particular intervention is truly helping a patient's mitochondria to function better.

Investigators also could take the tool in new directions. For example, CrCEST could be used to address one of Dr. McCormack's research questions: How does muscle mitochondria dysfunction contribute to precipitating diabetes?

"In order for me to study diabetes risk in these individuals, it's helpful to have a measure of muscle mitochondrial dysfunction," Dr. McCormack said. "Then, the next question is: 'Does muscle uptake of glucose depend on the degree of OXPHOS capacity?' And if it does, this might be an area to intervene to prevent the development of diabetes, in individuals with mitochondrial diseases as well as individuals with 'common' type 2 diabetes."



COLLABORATION

- 26 RESEARCHERS TEAM UP TO SOLVE CHALLENGES OF FVIII INHIBITORS IN PATIENTS WITH CONGENITAL HEMOPHELIA
- 27 CENTER OF EXCELLENCE FACILITATES CLINICAL TRIALS FOR PEDIATRIC KIDNEY DISEASE
- 28 IT TAKES A VILLAGE: COMMUNITY-BASED RESEARCH AIMS TO REDUCE ASTHMA DISPARITIES
- 29 THROUGH NEW COLLABORATION, CHOP ONCOLOGIST WORKS TO BETTER APPLY IMMUNE THERAPY

RESEARCHERS TEAM UP TO SOLVE CHALLENGES OF FVIII INHIBITORS IN PATIENTS WITH CONGENITAL HEMOPHILIA



Scientists have been puzzled for many years about why 20 to 30 percent of patients with hemophilia type A form inhibitory antibodies to protein replacement therapy that prevents it from working. With a new grant from the National Heart, Lung, and Blood Institute (NHLBI), [Valder Arruda, MD, PhD](#), a researcher in the Division of Hematology, developed a multi-pronged plan to test the problem from diverse perspectives and overlapping angles. The funding will support Children's Hospital of Philadelphia's establishment of one of three Centers for the Investigation of Factor VIII Immunogenicity.

Dr. Arruda, who also is an associate professor of Pediatrics at the [Perelman School of Medicine](#) at the [University of Pennsylvania](#), assembled a team of investigators at different stages of their careers and from a wide range of backgrounds — structural biology, immunology, genomics, and cancer immunotherapy — to launch the Center. It also will incorporate a skills development core to support the next generation of interdisciplinary scientists interested in building expertise in hemophilia.

"We need friends and colleagues from other areas who might help us to train the younger generation with different eyes rather than using the same typical approaches what we already know," Dr. Arruda said. "At CHOP, we have built a culture where the bridge between basic and clinical science is very big."

Clinicians in the [Hemophilia and Bleeding Disorders program](#) at CHOP provide care for about 100 boys with [hemophilia A](#), which is a lifelong disease caused by a lack of the blood clotting factor VIII. In order to maintain clotting factor levels, they may receive factor replacement infusions. Patients who form FVIII inhibitors in response to the therapy face serious obstacles that make it difficult and extremely expensive to treat their hemophilia, lead to complications such as joint disease, and increase mortality.

CHOP's new FVIII Center has four projects under way — each with a different and broad perspective — to reveal new mechanistic insights into the multiple facets of the immune response to FVIII, Dr. Arruda said. The investigators will share their progress and findings with the other two FVIII centers the NHLBI designated at Emory University and Temple University so that they can exchange ideas and refine each other's research questions related to FVIII immunogenicity.



CENTER OF EXCELLENCE FACILITATES CLINICAL TRIALS FOR PEDIATRIC KIDNEY DISEASE

Due to the rarity of kidney disease in children, collaboration between pediatric research institutions is critical for mounting efficient and effective clinical trials in nephrology. In 2018, with funding from the [National Institute of Diabetes and Digestive and Kidney Diseases](#), researchers in the Division of Nephrology at Children's Hospital of Philadelphia led the development of a new [Pediatric Center of Excellence in Nephrology](#) (PCEN) at CHOP, the first of its kind to be devoted to translational research and clinical trials for children with kidney disorders. In partnership with other regional and national children's hospitals, the PCEN seeks to address current barriers to clinical trial implementation.

"Kidney diseases are rare in children, which is a good thing," said [Susan Furth, MD, PhD](#), chief of the Division of Nephrology at CHOP. "But in order to find out if a treatment is effective, you really need to have a substantial number of children to enroll, and you have to get individuals at a number of centers to agree on things like the definition of who you will include in the study, how are you going to measure the outcomes of the study, and then get everybody to adhere to the protocols over time."

The PCEN's learning health system (LHS) core leverages electronic health records (EHR) across eight large children's hospitals through [PEDSnet](#), in order to identify pediatric patients with particular kidney disorders. With this information in hand, nephrology researchers can study patient outcomes, identify treatments that appear to be effective, and investigate specific laboratory markers that might predict who might or might not respond to a certain intervention. Ultimately, the EHR will allow researchers to recruit more patients into clinical trials. Alongside the LHS core, the PCEN houses a clinical phenotyping core focused on cardiovascular risk factors and measurements of growth and bone health, and also provides design and analysis expertise to the investigators making up the research base at CHOP, Penn, Johns Hopkins, and across the PEDSNet institutions.

In the PCEN's first year, two primary investigators have made significant progress utilizing the PCEN cores: [Michelle Denburg, MD, MSCE](#), attending physician in Nephrology at CHOP, leads a study of skeletal health in chronic kidney disease, while [Gregory Tasian, MD, MSc, MSCE](#), pediatric urologist at CHOP, investigates the use of ultrasound imaging of kidneys as a biomarker for how quickly a child's kidney might fail. In addition, the Center has fueled the design of future clinical trials with its launch of a [pilot feasibility program](#) and the award of two pilot grants and numerous mini-grants for study design and analysis support.

In the next five years, Dr. Furth hopes to see the PCEN mount clinical trials of new therapies for children with glomerular disease through a [glomerular disease learning network](#) (GLEAN) co-led by Dr. Denburg. Glomerular diseases are uncommon but can be extremely aggressive in terms of progressive kidney damage, and researchers in the network have already begun to lay the groundwork for clinical trials by coming together to standardize the data collected on patients.

A young boy with dark hair is shown in profile, using a green nebulizer mask over his nose and mouth. He is holding the device with his right hand. The background is slightly blurred, showing what appears to be a home setting with a window and some shelves.

IT TAKES A VILLAGE: COMMUNITY-BASED RESEARCH AIMS TO REDUCE ASTHMA DISPARITIES

More than 20 years ago, [Tyra Bryant-Stephens, MD](#), then medical director at a Children's Hospital of Philadelphia primary care center, learned from colleagues in the emergency department that children were visiting the ED with asthma-related problems at a concerning frequency. After pulling charts, probing practices, and talking with parents, Dr. Bryant-Stephens learned that the problem lay not in what primary care doctors prescribed, but in their communication with parents at home: Doctors could not address everything they needed to about managing asthma — a complex disease heavily influenced by a child's environment — in a 15- to 20-minute visit.

Nearly two decades later, after the implementation of home visits by community health workers, free asthma education classes across the city, and rigorous research to improve the way pediatricians support parents, particularly in low-income neighborhoods, the Community Asthma Prevention Program (CAPP) continues to thrive as a nationally recognized initiative. In June 2018, the U.S. Environmental Protection Agency bestowed to CAPP their prestigious [Leadership Award for Communities in Action in Asthma Management](#).

"The heart of CAPP are the home visits and education, and the heartbeat of CAPP are the community health workers who, by definition, understand the stresses of the community and know how to navigate it," said Dr. Bryant-Stephens, founder and medical director of CAPP. "Having said that, we are now trying to address every sector that the child is in, to utilize and collaborate with community partners to change the environment wherever they are."

Collaboration truly lies at the core of CAPP, and this is most strikingly evident in one of its most recent projects, the West Philadelphia Asthma Care Collaborative (WEPACC). In May 2018, the National Heart, Lung, and Blood Institute [named CAPP one of four grant recipients](#) tasked with developing sustainable programs to improve outcomes in communities with especially high rates of childhood asthma.

With the support of the grant, Dr. Bryant-Stephens and her team established a network of stakeholders representing public housing, community organizations, school districts, Medicaid managed-care companies, and more. The WEPACC network connects four sectors in childhood asthma care — the home, the community, medical professionals, and family — by utilizing community health workers. Through the project, Dr. Bryant-Stephens and her team study outcomes for 600 school-aged children with asthma assigned to one of four study arms: primary care community health workers, school community health workers (or "school ambassadors"), both primary care and school community health workers, and a control group. The community health workers will deliver patient-centered, evidence-based interventions developed by CAPP.

"One of the interesting outcomes may be finding which level of intervention is needed for different severities of the disease," Dr. Bryant-Stephens said. "A child with severe asthma may need the school ambassador-primary care connection more than somebody who only has occasional flares. As we're getting to personalized medicine and realizing that one size doesn't fit all, I hope that it helps us to see what works best for children."

Learn more about the [Community Asthma Prevention Program](#).



THROUGH NEW COLLABORATION, CHOP ONCOLOGIST WORKS TO BETTER APPLY IMMUNE THERAPY

The rapid pace of immune therapy advancements worries [David Barrett, MD, PhD](#), to some degree.

“Many, many drugs are coming forward that target the immune system,” said Dr. Barrett, a pediatric oncologist in the [Cancer Center at Children’s Hospital of Philadelphia](#). “Many of these drugs are tried in adult cancers, and have some success. The drugs are then applied to children and their unique cancers without any thought over whether that makes sense for their immune systems. I fear we will abandon immune therapies too quickly because they ‘don’t work’ when in reality we just didn’t apply them right.”

Conducting basic and translational research on samples from children with actual pediatric cancers will aid in applying immune therapy correctly, he said. To that end, Dr. Barrett has begun work on “Characterizing Immuno-variability in Children Following Standard of Care Treatment to Enable Precision Assignment to Immunotherapy Trials.”

He received the [2018 Stand Up to Cancer \(SU2C\) Phillip A. Sharp Innovation in Collaboration Award](#) with his collaborator, Trevor Pugh, PhD, a scientist at Toronto’s Princess Margaret Cancer Center. Dr. Barrett met Dr. Pugh for the first time at January’s SU2C Scientific Summit, which connects researchers and encourages them to forge new collaborations on the spot. CHOP oncology colleague [John Maris, MD](#), introduced the two because he thought their “techniques could be merged to do something more powerful,” recalled Dr. Barrett, noting they will receive \$125,000 annually for two years. “We talked and wrote the grant over two days.”

Through the funding, they will examine 100 children with cancer and analyze their immune systems with multiple complementary approaches using specialty assays they developed.

“These assays will help define which therapies each tumor type, or even possibly each child, might respond to so we can better apply the right therapy in the right context,” Dr. Barrett explained.

HONORS



- 32 A LIFE OF INNOVATION, DEDICATION, AND HEARTFELT CARE: REMEMBERING RAOBERT CAMPBELL, MD
- 33 COMING FULL CIRCLE: STEVEN HUNGER, MD, RECEIVES LECTURESHIP AWARD FROM EARLY SUPPORTER
- 34 NOVEL INSIGHTS: CUTTING-EDGE TECHNIQUES LEADS JASON VAN BATAVIA, MD, TO NEURO-UROLOGY HONOR
- 35 VACCINE CHAMPION: SABIN GOLD MEDAL BESTOWED ON PAUL OFFIT, MD
- 36 A RESEARCH TRIFECTA: ELIZABETH BHOJ, MD, PhD RECEIVES THREE MAJOR AWARDS
- 37 A PATH FOR DISCOVERY: JORGE HENAO-MEJIA, MD, PhD, WINS PATHOGENESIS OF INFECTIOUS DISEASE AWARD
- 38 FROM BENCH TO BEDSIDE: SARAH HENRICKSON, MD, PhD, HONORED WITH CAREER AWARD
- 39 IN THE SPOTLIGHT: CELEBRATING THE RESEARCH LEGACIES OF BARBARA SCHMIDT, MD, AND HARESH KIEPALANI, MD
- 40 HONORING INNOVATION: STEPHAN GRUPP, MD, PhD, RECEIVES CITIZEN DIPLOMAT OF THE YEAR AWARD

- 41 CELEBRATING YOUNG INVESTIGATORS: NATIONAL KIDNEY FOUNDATION HONORS MELISSA MEYERS, MD
 - 42 IGNACIO TAPIA, MD, RECEIVES OUTSTANDING ACHIEVEMENT AWARD
 - 43 KRISTY ARBOGAST, PHD, RECEIVES AWARD FOR EXCELLENCE IN MENTORING RESEARCH TRAINEES
 - 44 KATHLEEN SULLIVAN, MD, PHD, RECEIVES MULTIPLE AWARD IN FIELD OF IMMUNOLOGY
-

A portrait of Dr. Robert Campbell, MD, a man with glasses and a surgical cap, wearing a white lab coat. He is standing in front of a modern building with large windows. The image is partially obscured by a white text box on the left.

A LIFE OF INNOVATION, DEDICATION, AND HEARTFELT CARE: REMEMBERING ROBERT CAMPBELL, MD

After a lifetime of innovation and care, world-renowned pediatric orthopaedic surgeon Robert Campbell, MD, passed away peacefully in July. A true innovator, Dr. Campbell's thought-leadership and inventions changed the care for children with complex and life-threatening spine and chest wall deformities. He is best known as the inventor of the [vertical expandable prosthetic titanium rib](#), or VEPTR, the first device approved by the FDA to treat [thoracic insufficiency syndrome](#) (TIS), a rare congenital condition affecting children in which the thorax cannot support regular growth or breathing. By [separating the ribs](#) and helping to straighten the spine, the VEPTR is designed to give children's lungs room to grow, allowing them to breathe without the aid of ventilators. Left untreated, TIS can be devastating. As children with TIS grow, the condition causes the chest wall to become deformed and can ultimately lead to death due to respiratory insufficiency. However, since Dr. Campbell implanted the first VEPTR in 1989, the device has proven to be a lifesaver. His invention has become the standard of care throughout the world, saving or extending the lives of children with previously untreatable conditions.

Dr. Campbell led a [Journal of Pediatric Orthopaedics](#) study that showed the VEPTR treatment improved Jeune syndrome (a severe form of TIS) patients' survival to nearly 70 percent, compared to a 70 to 80 percent mortality rate without treatment.

But his contributions didn't stop with the development of VEPTR. After joining Children's Hospital in 2008, he launched CHOP's [Center for Thoracic Insufficiency](#), attracting children from around the world, many of whom were told "nothing can be done." He created a team approach to care, collaborating closely with pulmonologists, thoracic surgeons, intensivists and radiologists to optimize treatment of children with severe spine and chest wall deformities. In addition, his innovation formed the basis of a new [CHOP Frontier Program](#) to improve outcomes for patients with TIS.

Dr. Campbell traveled worldwide, training surgeons in the use of VEPTR and assisting them with their most difficult cases while consistently and compassionately caring for patients and their families. He was the recipient of numerous awards for his innovations over the course of his career, including the [Life Sciences Pennsylvania's \(formerly Pennsylvania Bio\) Patient Impact Award](#). Shortly before his passing, the National Organization for Rare Disorders Inc. honored him and his pioneering work with their [Lifetime Achievement Award](#).



COMING FULL CIRCLE: STEVEN HUNGER, MD, RECEIVES LECTURESHIP AWARD FROM EARLY SUPPORTER

The past several decades have witnessed a dramatic shift in the landscape for how curable some pediatric cancers are, especially acute lymphoblastic leukemia (ALL), which was once incurable and now has about a 90 percent cure rate. ALL has been the central focus of the research of [Stephen P. Hunger, MD](#), and his pioneering investigations led the [American Society of Pediatric Hematology/Oncology](#) (ASPHO) to award him with the [George R. Buchanan Lectureship Award](#) in May 2018.

The award had a particularly special meaning for Dr. Hunger, who serves as chief of the [Division of Oncology](#) and director of the [Center for Childhood Cancer Research](#) at CHOP. That's because Dr. George R. Buchanan—past president of ASPHO and a renowned pediatric hematology physician-researcher—was supportive of Dr. Hunger early in his career. “I was both flattered and honored,” Dr. Hunger said of the distinction. “He helped me to get established nationally.” Dr. Hunger accepted the award at the ASPHO Conference in May, where he personally thanked Dr. Buchanan and presented a lecture on improving survival for children and young adults with [acute lymphoblastic leukemia](#).

Dr. Hunger [shared his perspective](#) on receiving the award and the future of pediatric cancer research, enthusiastic about the promise of more targeted therapies that have a better “therapeutic index”—meaning they have much more specificity in terms of leukemia cell killing while sparing the normal cells and therefore reducing the side effects to treatment. He also expressed hope about incorporating immunotherapy into ALL treatment to perhaps lead to better cure rates and potentially allowing physicians to move beyond some aspects of current therapy.

NOVEL INSIGHTS: CUTTING-EDGE TECHNIQUES LEADS JASON VAN BATAVIA, MD, TO NEURO-UROLOGY HONOR



Cutting-edge neuroscience techniques are leading to a better understanding of the brain's role in controlling bladder function, and the novel insights of one CHOP investigator earned him special recognition from the neuro-urology community.

[Jason Van Batavia, MD](#), a urologist and physician-scientist in the Division of Urology, [was named the grand prize winner](#) in the [2018 Diokno-Lapides Essay Contest](#). His manuscript described a research project focused on optogenetic stimulation of specific neurons in a section of the brainstem called Barrington's nucleus, which scientists think is an important "command center" for controlling voiding (urination).

Identifying these neurons' role in voiding could help scientists to figure out new approaches to treating voiding dysfunction in children. Forty percent of children — that's around 2,000 new patients a year — who visit CHOP's [DOVE Center for Voiding and Bladder Function](#) have lower urinary tract symptoms, which include high urination frequency or leakage of urine during the day or night.

"Those are some of the most common problems that we see in the pediatric urology world," said Dr. Van Batavia, who also is a clinical instructor of Urology at the [Perelman School of Medicine](#) at the [University of Pennsylvania](#). "And yet our understanding of them hasn't changed much in the last few decades."

The optogenetic stimulation approach Dr. Van Batavia employed involves using light to selectively control cells of interest. The results of his study point to the CRH expression in the brain, and CRH receptor activity may be a key factor in some dysfunctional voiding patterns. These novel insights led him to receive the prestigious prize May 19 at the [American Urological Association Annual Meeting](#). Dr. Van Batavia's work involved mentoring and guidance from [Stephen Zderic, MD](#), pediatric urologist at CHOP; [Rita Valentino, PhD](#), former director of the Stress Neurobiology Division within the Department of Anesthesiology at CHOP, as well as support from the Division of Urology under the leadership of [Douglas Canning, MD](#), chief of the Division of Urology at CHOP.



VACCINE CHAMPION: SABIN GOLD MEDAL BESTOWED ON PAUL OFFIT, MD

Throughout his decades-long career as a researcher, author, professor, vaccine advocate, and strident spokesperson for accurate science, [Paul Offit, MD](#), has been the recipient of numerous awards. In 2018 he added “gold medalist” to his vibrant list of honors and accolades, when he [received the 2018 Albert B. Sabin Gold Medal](#) from the [Sabin Vaccine Institute](#).

The Sabin Gold Medal recognizes individuals who have made significant contributions in vaccinology or complementary fields. The annual award commemorates the legacy of Dr. Albert B. Sabin, renowned scientist and inventor of the oral live virus polio vaccine that nearly eradicated polio worldwide.

As the 25th recipient of the Sabin Gold Medal, Dr. Offit received the award for his co-invention of an oral rotavirus vaccine, and his leadership as “one of the United States’ most vocal and dedicated advocates for immunization,” [according to the Sabin Vaccine Institute](#).

“It’s an honor to join the distinguished ranks of Albert B. Sabin Gold Medal recipients,” Dr. Offit said. “Though our research may have focused on different diseases, we all share Dr. Sabin’s commitment to reducing human suffering.”

Dr. Offit, who directs the [Vaccine Education Center](#) at Children’s Hospital and holds the Maurice R. Hilleman Chair of Vaccinology, worked tirelessly with his colleagues on the vaccine for 26 years before it was brought to the marketplace, where it quickly proved its effectiveness and has since reduced child hospitalizations from rotavirus by 85 percent.

Beyond his work on vaccines, Dr. Offit is equally renowned for speaking up and writing about the importance of clear science communication and critical thinking, particularly when it comes to central issues in children’s health like vaccine safety and immunization.

A RESEARCH TRIFECTA: ELIZABETH BHOJ, MD, PhD RECEIVES THREE MAJOR AWARDS



Winning a trio of major distinctions in one month is certainly a rare feat, clinical geneticist [Elizabeth Bhoj, MD, PhD](#), modestly admits, but one she is proud of, and so are we. In May, Dr. Bhoj, whose area of expertise is in the field of translational genomics, earned the William K. Bowes Jr. Award in Medical Genetics, the Burroughs Wellcome Fund's Career Awards for Medical Scientists with a \$700,000 prize, and the Society for Pediatric Research's (SPR) Physician Scientist Award.

Dr. Bhoj received the SPR award in Toronto at the Pediatric Academic Societies Meeting where she presented the lecture "Novel Gene Discovery in a Cohort of Patients with Craniofacial and Neurologic Syndromes."

She has conducted soon-to-be-published research on histone 3.3. Histones are proteins that wrap around DNA to keep it organized. Dr. Bhoj and colleagues found that a mutation in this particular histone is associated with a novel phenotype of developmental delay, neurodegeneration, epilepsy, and facial dysmorphism.

In other research, Dr. Bhoj has played a key role in the CHOP team who discovered a new growth disorder, [Mulchandani-Bhoj-Conlin Syndrome](#). Named in recognition of their work, the condition — characterized by failure to thrive, severe short status, and profound feeding difficulties — is caused by an abnormality of chromosome 20.

Referring to the award triple-play, Dr. Bhoj said, "Having this vote of confidence is even more important than the financial support. Getting the feedback of, 'Yes, we believe in you; this work has value, and it should continue,' is an enormous career boost."



A PATH FOR DISCOVERY: JORGE HENAO-MEJIA, MD, PhD, WINS PATHOGENESIS OF INFECTIOUS DISEASE AWARD

Whether from a mentor or the larger scientific community, recognition and support go a long way toward propelling the careers of new investigators working to establish research programs that may lead to tomorrow's breakthroughs.

With a dedication toward advancing the biomedical sciences, the [Burroughs Wellcome Fund](#) (BWF) is an independent foundation that provides highly competitive awards to investigators in the early stages of their research careers. One of those annual awards is the Pathogenesis of Infectious Disease (PATH) Award, which this year [BWF awarded](#) to [Jorge Henao-Mejia, MD, PhD](#), assistant professor of Pathology and Laboratory Medicine at CHOP.

The [PATH Award](#) provides investigators at the assistant professor level with the opportunity to bring multidisciplinary approaches to the study of human infectious diseases. Supported by a \$500,000 grant over five years, Dr. Henao-Mejia is continuing his investigation of the critical role that [the microbiota](#) — that vast population of bacteria and other microorganisms living within the human gastrointestinal tract — play in obesity and type 2 diabetes.

It's well-established that the microbes in our gut help to regulate a number of physiological processes and, when dysregulated, can contribute to the development of highly prevalent disorders. Factors like lifestyle, age, diet, antibiotic exposure, and genetics can all contribute to an individual's unique microbiota composition.

But despite recent advances in its role in disease, the detailed mechanisms by which the microbiota promotes obesity and type 2 diabetes are still poorly understood, a gap in knowledge Dr. Henao-Mejia is working to fill with the support of the PATH Award. Besides the award's financial support, Dr. Henao-Mejia said that being selected for the award holds special meaning when it comes to his career trajectory, too.

"To be supported for projects that are considered high-risk, high-reward is very important when [a researcher] is starting an independent career," he said. "I think it's very valuable that BWF is willing to invest in young investigators, and it's a wonderful initiative. I feel very lucky, privileged, and grateful for being part of a select group of people."

FROM BENCH TO BEDSIDE: SARAH HENRICKSON, MD, PhD, HONORED WITH CAREER AWARD



It takes the right mix of innovative thinking, passion, and persistence for young investigators to succeed in research. But another key ingredient for the kind of success that can lead to tomorrow's discoveries is the support these investigators receive early in their careers. Such support can take numerous forms, including recognition and awards from the scientific community.

The [Burroughs Wellcome Fund](#) (BWF), an independent foundation dedicated to advancing biomedical science, bestowed its prestigious Career Award for Medical Scientists (CAMS) to [Sarah Henrickson, MD, PhD](#), for her groundbreaking work on [how the immune system functions](#) in pediatric disease, in particular inflammatory diseases like asthma and obesity. Specifically, Dr. Henrickson addresses the question of whether obesity might affect how a child with asthma responds to a vaccine.

[The CAMS Award](#) supports scientists early on in their careers, providing significant funding over a five-year period to physician-scientists on an academic career track and who are in the early years of their research careers.

With the support of the CAMS Award, Dr. Henrickson aims to start her own independent research group and continue to identify new hypotheses of mechanisms of immune dysfunction in pediatric disease while starting to validate the mechanisms found in her earlier work. As an allergist/immunologist, Dr. Henrickson's overarching goal is to improve the outcomes of the patients she sees in the clinic based on a more mechanistic understanding of what underlies their different diseases.

"I'm really focused on bringing together different kinds of data, from clinical to genomic, to learn as much as possible, and always going back to the clinical data so that we're relevant to the issue of the patient and their disease," Dr. Henrickson said.

Dr. Henrickson was one of two CHOP investigators to receive the CAMS award this past year, the second going to clinician-researcher Elizabeth Bhoj, MD, PhD, for her research in translational [genomics](#). BWF also recognized [Jorge Henao-Mejia, MD, PhD](#), assistant professor of Pathology and Laboratory Medicine at CHOP, with its [Pathogenesis of Infectious Disease Award](#).

Also during the fiscal year, Dr. Henrickson received a [2018 Faculty Development Award](#) from the American Academy of Allergy, Asthma and Immunology Foundation for her work into immunometabolic alterations in primary immunodeficiency.

A photograph of four people standing together in front of an American flag. From left to right: a woman with short brown hair wearing a purple top, a man with glasses wearing a dark suit and red tie, an older woman with short white hair wearing a light-colored patterned jacket, and a man with glasses wearing a tan suit and striped tie. The background is a dimly lit room with a desk and a lamp visible on the left.

IN THE SPOTLIGHT: CELEBRATING THE RESEARCH LEGACIES OF BARBARA SCHMIDT, MD, AND HARESH KIEPALANI, MD

The remarkable accomplishments of two neonatal research and medicine pioneers took center stage in May 2018 as the [Division of Neonatology](#) celebrated the careers and retirements of Barbara Schmidt, MD, and Hareesh Kirpalani, MD. The Division held a [clinical research symposium](#) that brought together the world's leading experts in neonatal research and evidence-based medicine, many of whom had worked closely with Drs. Schmidt and Kirpalani as trainees, co-authors, and colleagues in the last few decades.

Together, Drs. Schmidt and Kirpalani devoted more than 30 years to driving evidence-based neonatal research forward and training the next generation of the field's researchers. Dr. Schmidt, who was an attending neonatologist at CHOP and director of Neonatology Clinical Research at Penn Medicine, had led a host of collaborations and clinical trials in newborns, including the International Trial of Caffeine for Apnea of Prematurity. In 2017, the American Academy of Pediatrics [honored Dr. Schmidt with the William A. Silverman Lectureship Award](#), and in 2015, she received the prestigious Order of Canada.

Dr. Kirpalani, who was an attending neonatologist at CHOP and Emeritus Professor CE of Pediatrics at Penn Medicine, made critical contributions to advancing neonatal clinical trials as well as to ethics and decision-making in newborn medicine. Dr. Kirpalani co-founded the [International Society for Evidence-Based Neonatology](#), a nonprofit organization that promotes the belief that neonatal care should be firmly built on the best available evidence. In 2015, Dr. Kirpalani was named CHOP Mentor of the Year.

The symposium in their honor featured investigators from institutions around the world and concluded with another honor when [Eric Eichenwald, MD](#), chief of the Division of Neonatology, announced the new Schmidt-Kirpalani Mentorship Award. The award, to be presented annually, is an ode to the extensive mentoring work of Drs. Schmidt and Kirpalani and celebration of their [decades-long research legacy](#).



HONORING INNOVATION: STEPHAN GRUPP, MD, PhD, RECEIVES CITIZEN DIPLOMAT OF THE YEAR AWARD

His groundbreaking research over nearly two decades has led to numerous awards for [Stephan Grupp, MD, PhD](#), a pediatric oncologist who maintains an unwavering commitment to improving the lives of children battling different forms of cancer by changing the standard of care for these diseases. He recently added another honor to his growing list when the Citizen Diplomacy International of Philadelphia, a nonprofit international relations organization, awarded him with the [2018 Citizen Diplomat of the Year Award](#).

The award recognized Dr. Grupp for “raising Philadelphia’s international profile through his innovative advancements in medicine and his commitment to ensuring that people all around the world have access to this treatment.”

In collaboration with the Perelman School of Medicine and Novartis, Dr. Grupp led U.S. global clinical trials of the innovative life-saving chimeric antigen receptor (CAR) T-cell therapy for children with advanced acute lymphoblastic leukemia. This breakthrough garnered international attention and brought newfound promise to those with cancer, and in August 2017 the Food and Drug Administration [approved this game-changing cellular therapy](#) to treat cancer with a patient’s own immune system. Tisagenlecleucel, the first therapy and the first engineered cell therapy ever approved by the agency, targets patients age 25 and under who have an aggressive form of this type of leukemia, the most common cancer of childhood.

Dr. Grupp directs the Cancer Immunotherapy Program at CHOP, as well as the translational research of the [Center for Childhood Cancer Research](#) and the Stem Cell Laboratory. He continues his innovative research into new cell therapies while maintaining an active schedule with his patients, and traveling the world to educate doctors and other providers about safe use of this new cancer immunotherapy.



CELEBRATING YOUNG INVESTIGATORS: NATIONAL KIDNEY FOUNDATION HONORS MELISSA MEYERS, MD

The [National Kidney Foundation's National Young Investigator's Forum](#) proved to be a powerful and rewarding experience for Melissa Meyers, MD, for two reasons. First, she won first place in the clinical research section for her talk about increased risk in children receiving renal transplants. Second, the third-year nephrology fellow sat in exclusive company as the only pediatrician in the room.

“Increased Risk” refers to a donor’s increased risk of transmitting a blood-borne infection — especially hepatitis B and C and HIV. This broad Increased Risk category, which has evolved over the years, now could contain anything from a history of incarceration for more than 72 hours over the last year to IV drug use, an unfortunate result of the nation’s current opioid epidemic.

About 20 percent of the deceased donor pool is flagged nationally as Increased Risk, and in some regions the rate jumps to nearly one-third. Despite having a lot of information on how adults receive these organs, there is a paucity of similar information for children, and Dr. Meyers wanted to see how often kids receive these organs. What she found was that Increased Risk kidneys were more frequently transplanted into adult patients. Her study led the National Kidney Foundation to [give her top honors](#) during their April 2018 forum after an open competition judged by independent clinical experts.

In her talk during the event, Dr. Meyers expressed her enthusiasm to focus on what kids are going through, and to share those insights with practitioners who primarily care for adult patients.

“I told the audience, ‘I want to take you in another direction and look at things through a different lens. We want to protect our kids as much as possible and offer them the best possible organs,’” Dr. Myers said.

IGNACIO TAPIA, MD, RECEIVES OUTSTANDING ACHIEVEMENT AWARD



Children's Hospital of Philadelphia's [Ignacio Tapia, MD](#), was humbled to receive the first [Carole L. Marcus Outstanding Achievement Award](#) from the American Thoracic Society (ATS). The award is named in honor of Dr. Tapia's mentor and CHOP colleague who was a leader in pediatric sleep medicine research.

Dr. Marcus, who died in 2017, served as director of CHOP's Sleep Center and the Clinical and Translational Research Center/Center for Human Phenomic Science. She was associate director of the Institute for Translational Medicine and Therapeutics at the University of Pennsylvania. Dr. Tapia and Dr. Marcus frequently collaborated on research projects and publishing papers reporting their results.

Dr. Tapia, an attending pulmonologist in the Division of Pulmonary Medicine at CHOP, is committed to helping shape the future of pediatric pulmonary and sleep medicine. His research focuses on understanding the central nervous system complications of obstructive sleep apnea (OSA) in children. He also serves as the director of [CHOP's Pulmonary Medicine Fellowship Program](#) and is an assistant professor of Pediatrics at the [Perelman School of Medicine](#) at the [University of Pennsylvania](#).

Dr. Tapia accepted the award in May at the 2018 ATS International Conference in San Diego. "It was a great honor to receive this award named after my mentor. I am working hard every day to live up to the expectations," he said.



KRISTY ARBOGAST, PhD, RECEIVES AWARD FOR EXCELLENCE IN MENTORING RESEARCH TRAINEES

The path to becoming an internationally recognized bioengineer with a focus on brain injury mechanics wasn't straightforward for [Kristy Arbogast, PhD](#). She had to find creative ways to apply her scientific skills as a non-clinician researcher at a pediatric hospital. Today, when she mentors research trainees with diverse backgrounds and interests, she not only teaches them how to conduct excellent research, but also how to be adaptable and resourceful.

In recognition for being a consummate researcher-teacher who has influenced countless undergrads and mentored dozens of graduate students, post-docs, and fellows, Dr. Arbogast received the Award for Excellence in Mentoring Research Trainees. The award recognizes faculty members who effectively guide the training and professional development of early career investigators.

Her mentoring style, as reflected in one of her nomination letters, gives guidance while encouraging young researchers to pursue their independence: "An effective combination of autonomy and supervision is difficult for any mentor; however, Professor Arbogast is able to achieve the appropriate balance, which in my case allows me the freedom to explore my own research interests within the confines of a larger project."

Dr. Arbogast knows firsthand the value mentors have in shaping how CHOP investigators learn to interrogate a scientific problem, analyze the data, and use the results to improve the world. In 1997, she was one of the first research scientists hired by [Flaura Winston, MD, PhD](#), and [Dennis Durbin, MD, MSCE](#), who were starting the [Center for Injury Research and Prevention](#) (CIRP). Dr. Arbogast also had excellent mentorship from [Kathy Shaw, MD, MSCE](#), who was chief of the Division of Emergency Medicine when Dr. Arbogast started her faculty appointment.

"All of these individuals as mentors treated me as a person who could have a substantial contribution," Dr. Arbogast said. "I never once felt that my voice wasn't heard or they weren't interested in what I had to say. That carries over to how I conduct my mentor-mentee relationships. I want to hear from the mentees and welcome what they have to say." Dr. Arbogast is the co-scientific director and director of Engineering at CIRP, and co-director of the [Center for Child Injury Prevention Studies](#). She also is R. Anderson Pew Distinguished Chair of Pediatrics at CHOP and a professor of Pediatrics at the [Perelman School of Medicine](#) at the [University of Pennsylvania](#).



KATHLEEN SULLIVAN, MD, PhD, RECEIVES MULTIPLE AWARD IN FIELD OF IMMUNOLOGY

Chief of the Division of Allergy and Immunology at Children’s Hospital of Philadelphia, [Kathleen Sullivan, MD, PhD](#), received recognition — both inside and outside of CHOP — for her research and contributions in the field of primary immunodeficiency diseases, and for her mentorship of up-and-coming investigators.

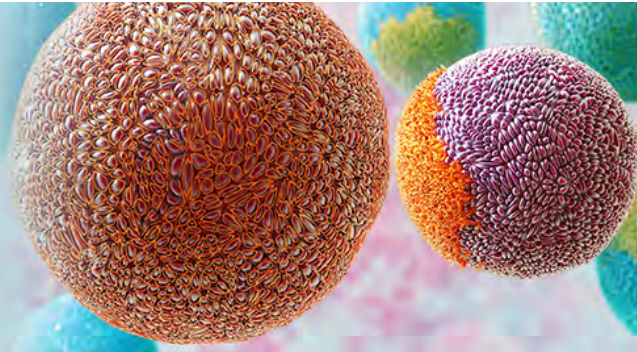
During the 2017 Immune Deficiency Foundation National Conference in Anaheim, Calif., Dr. Sullivan was given the [Boyle Scientific Achievement Award](#). The recognition was for her accomplishments in investigating common variable immunodeficiency, chromosome 22q11.2 deletion syndrome, and her work in defining the role of epigenetics in inflammation.

“The Boyle Award is the highest honor in the field of primary immune deficiency, and I was thrilled to be recognized,” Dr. Sullivan said.

Closer to home, Dr. Sullivan, who also holds the Frank R. Wallace Endowed Chair in Infectious Diseases, and is a professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania, was the recipient of the 2018 CHOP Faculty Mentor Award. The Research Institute’s Office of Faculty Development presents the award as an honor to faculty investigators whose mentoring has helped to produce the next generation of investigators dedicated to child health discoveries and clinical practice breakthroughs.

In a nomination letter from current and former divisional faculty of Allergy and Immunology, Dr. Sullivan’s colleagues wrote, “Although always stage-specific, her approach to mentorship is consistently thoughtful and practical: Set goals, prioritize tasks, and collaborate across disciplines whenever possible. It is a winning strategy.”

VISIONARIES



- 46 NEW ASSISTANT VICE PRESIDENT AND CHIEF CLINICAL RESEARCH OFFICER: RICHARD APLENC, MD, PhD, MSCE
- 47 FOSTERING COLLABORATION WITH THE RUTH M. COLKET ENDOWED CHAIR IN PEDIATRIC NURSING: MARTHA A. Q. CURLEY, RN, PhD, FAAN
- 48 FIRST ASSOCIATE VICE PRESIDENT AND CHIEF RESEARCH INFORMATICS OFFICER: JEFF PENNINGTON
- 49 NEW CHIEF OF ENDOCRINOLOGY AND DIABETES: DIVA DE LEON-CRUTCHLOW, MD, MSCE
- 50 SAVVAS ANDRONIKOU JOINS RADIOLOGY DEPARTMENT AS VICE CHAIR OF CLINICAL RESEARCH

NEW ASSISTANT VICE PRESIDENT AND CHIEF CLINICAL RESEARCH OFFICER: RICHARD APLENC, MD, PHD, MSCE



[Children's Hospital of Philadelphia Research Institute](#) welcomed [Richard Aplenc, MD, PhD, MSCE](#), as assistant vice president and chief clinical research officer in early 2018. A long-standing member of the CHOP research community, Dr. Aplenc's work at [CHOP](#) began with his Pediatric Hematology Oncology Fellowship in 1997. A faculty member since 2002, Dr. Aplenc currently is a professor of both Pediatrics and Epidemiology at the Perelman School of Medicine at the University of Pennsylvania. In his new leadership role, Dr. Aplenc is setting the course for the development and oversight of clinical research operations across CHOP.

Dr. Aplenc's research is focused on [acute myeloid leukemia](#) (AML), chiefly AML therapeutics as well as clinical and genetic epidemiology studies that aim to improve clinical outcomes for pediatric patients. Dr. Aplenc received a Hyundai Quantum Grant from Hyundai Hope on Wheels in 2016 to identify novel cell surface proteins for immunotherapy targeting and is leading a Phase I chimeric antigen receptor (CAR) trial in the [Pediatric Blood and Marrow Transplant Consortium](#).

He is also using "big data" to improve the care of children with AML today. These projects use very large data sets to identify patient populations at particular risk for chemotherapy side effects. Dr. Aplenc is interested in understanding the risk factors associated with cardiac complications during and shortly after AML therapy. In addition, he is studying why certain demographic groups of patients seem to be at increased risk of toxicity and death during AML therapy. This work is leading his research group into analyses of patient-reported outcomes and preferences as we seek to understand the experience of patients and families undergoing AML therapy in the United States.

Finally, Dr. Aplenc leads a multi-centered prospective clinical trial evaluating medical and patient-reported outcomes for different hospitalization strategies after AML chemotherapy in children. This work is funded by the [Patient-Centered Outcomes Research Institute](#).

His broad research experiences reflect the commitment of all of the investigators at CHOP Research to improve outcomes for pediatric patients, while his immersion in Phase I clinical trials has uniquely prepared Dr. Aplenc to lead his team through the thrilling but sometimes choppy waters of discovery. Whether working to reveal new molecular mechanisms or unraveling the complexities of conducting drug therapy trials, Dr. Aplenc is inspired by families and patients living with life-threatening illness who choose to participate in research to give other children a chance at healthier futures.

FOSTERING COLLABORATION WITH THE RUTH M. COLKET ENDOWED CHAIR IN PEDIATRIC NURSING: MARTHA A. Q. CURLEY, RN, PHD, FAAN



Our nurse scientists offer a unique perspective that strengthens our clinical care practices and improves our pediatric patients' outcomes. In the interest of continued collaborative nursing research in child health across the University of Pennsylvania School of Nursing and [Children's Hospital of Philadelphia](#), [Martha A. Q. Curley, RN, PhD, FAAN](#) was appointed to the Ruth M. Colket Endowed Chair in Pediatric Nursing at CHOP. Dr. Curley holds a joint appointment in Anesthesia and Critical Care Medicine at the Perelman School of Medicine.

Dr. Curley's decades of studies have informed the practice of caring for critically-ill patients with acute respiratory failure, highlighted relationship-based care when partnering with parents of critically-ill children, and supported parent presence during invasive procedures and resuscitation. Among the outcomes of Dr. Curley's work are the development and dissemination of [core metrics](#) in the field of pediatrics such as the State Behavioral Scale (SBS) to assess sedation of infants and children on ventilators, the Withdrawal Assessment Tool (WAT-1) to assess opioid and benzodiazepine withdrawal, Individualized Numeric Rating Scale (INRS) for the assessment of pain levels in children unable to speak, and the Braden QD scale for predicting pressure-related skin injuries in hospitalized children.

Dr. Curley's impactful research continues with a recent National Institutes of Health grant award for a clinical trial to support best practices in treating children with severe pediatric acute respiratory distress syndrome (PARDS). The 45-site randomized, controlled trial, ["PROSpect: Prone and Oscillation Pediatric Clinical Trial,"](#) is expected to provide definitive evidence for a major change in clinical practice for patients with severe PARDS. Dr. Curley is also investigating how nurses can create environments conducive to healing in pediatric intensive care units (ICUs) by embedding elements of the child's usual activity and modulating both light and noise during patients' ICU stay.

On the clinical side, Dr. Curley helped to develop the American Association of Critical-Care Nurses Synergy Model for Patient Care, which is now integrated into nursing curricula and the association's credentialing programs, linking evidence-based clinical practice with patient outcomes.

She encourages the next generation of nurse researchers by involving nursing students in her clinical inquiry activities.

FIRST ASSOCIATE VICE PRESIDENT AND CHIEF RESEARCH INFORMATICS OFFICER: JEFF PENNINGTON



Health informatics experts are in the exhilarating position to work at the intersection where copious volumes of data and its applications in pediatric care and research meet. In April 2018, [Jeff Pennington](#) became the first Associate Vice President and Chief Research Informatics Officer (CRIO) at Children's Hospital of Philadelphia Research Institute. In this newly created role, he is an integral member of the CHOP Research Institute Senior Leadership team and will ensure CHOP Research is the industry leader in use of data and technology to solve challenging problems in child health.

As CRIO, Pennington will partner with colleagues across CHOP to launch the exciting [Arcus program](#), a strategic investment in enterprise data, technology, and data science infrastructure that links all of CHOP's clinical and research data. The program is a key component of the CHOP Research Strategy, enabling next-generation computational biology, machine learning, and translational research.

At its heart, Arcus is a one-of-its-kind library based on all of the data generated at CHOP over the course of patients' clinical encounters and research study visits to produce a more holistic picture of pediatric health and disease, all while vigorously protecting our patients' right to privacy. More than a digital catalog, Arcus includes an educational component to help CHOP's research community become more capable and confident in the use of large, complex data sets.

Previously a leader in the CHOP Department of Biomedical and Health Informatics, Pennington recognizes the remarkable opportunity to deliver breakthrough, compassionate care when supported by a digital health enterprise that has been using a single electronic health record since 2010. This unique ability to leverage CHOP data through Arcus provides opportunities for pediatric medical innovation like nowhere else in the world.



NEW CHIEF OF ENDOCRINOLOGY AND DIABETES: DIVA DE LEON-CRUTCHLOW, MD, MSCE

It requires a unique individual to take the helm of one of the most robust clinical divisions at Children's Hospital of Philadelphia and one of the top-ranked pediatric divisions in the nation to boot. The ideal candidate generally possesses a combination of outstanding work as a physician-scientist; exemplary leadership skills; dedication to patients, families, and colleagues; and a commitment to education.

In July 2018, CHOP [honored one of its veteran physician-scientists](#) when it appointed [Diva De León-Crutchlow, MD, MSCE](#), as chief of the Division of Endocrinology and Diabetes. In her two decades at Children's Hospital, Dr. De León-Crutchlow has established an impressive and world-renowned clinical reputation and serves as director of CHOP's [Congenital Hyperinsulinism Center](#).

As a scientist, Dr. De León-Crutchlow has made significant advances into understanding [congenital hyperinsulinism \(HI\)](#) and monogenic diabetes. Her research focuses on HI pathophysiology, including the identification of a key biological target in HI treatment, glucagon-like-peptide-1 receptor (GLP-1). Her preclinical and clinical work has shown that exendin-(9-39), a compound that inhibits GLP-1 receptor, can prevent low blood sugar in HI. Her combination of clinical expertise and research innovation has led her to make significant strides in improving the health of children and adults with HI and developing novel therapies for the rare genetic condition.



SAVVAS ANDRONIKOU JOINS RADIOLOGY DEPARTMENT AS VICE CHAIR OF CLINICAL RESEARCH

[Savvas Andronikou, MBBch \(Wits\), PhD \(UCT\), PhD \(Wits\), FRCR \(Lond\), FCRad \(Diag\)](#), joined Children's Hospital in June as the vice chair of Clinical Research in the Department of Radiology, which has a flourishing research program that uses state-of-the-art technologies to disseminate innovative work in imaging for infants, children, and pregnant women.

In his role as vice chair, Dr. Andronikou helps oversee a growing translational and clinical research program in the department that is broadly related to and impacts nearly every pediatric subspecialty. It includes interventional radiology, cardiovascular, lymphatic imaging, pulmonary imaging, and oncology, among many others.

Dr. Andronikou serves as a critical leader for the department while maintaining his own robust research program. Because of his experience in imaging pediatric pulmonary disorders, he has been tasked to spearhead advanced pulmonary imaging and research in the department, as the director of the section of pulmonary imaging. In addition to earning two PhDs and acquiring extensive experience in both pediatric body imaging and pediatric neuroradiology training, Dr. Andronikou has contributed to more than 270 publications, written six books, and has vast experience in the organization of dedicated pediatric radiology research infrastructure and support.

He works in parallel to Timothy Roberts, PhD, vice chair for Imaging Research and Oberkircher Family Chair in Pediatric Radiology, and aims to create strong and seamless collaborations with PhD scientists in the department. In addition, Dr. Andronikou provides key support for the department's overall research strategy and has specific responsibility for the newly created Radiology Research Core.

DISCOVERY



- 53 INGESTING HONEY AFTER SWALLOWING BUTTON BATTERY REDUCES INJURY AND IMPROVES OUTCOMES
- 54 CHILDREN WITH CURRENT ALLERGIES SHOULD BE SCREENED FOR A CHRONIC FOOD ALLERGY
- 55 ORAL ANTIBIOTICS MAY RAISE RISK OF KIDNEY STONES
- 56 IN SEVERE CHILDHOOD NEURODEGENERATION, NOVEL MECHANISM FOUND
- 57 TARGETING A BRAIN CIRCUIT LED TO 'ANTIDEPRESSIVE' BEHAVIOR IN ANIMAL MODELS
- 58 IN HUNTINTON'S DISEASE, HEART PROBLEMS SHED LIGHT ON DISEASE PROGRESS
- 59 TEEN DRIVERS WITH ADHD SYMPTOMS HAVE MORE RISKY DRIVING BEHAVIORS
- 60 'MISSING MUTATION' FOUND IN SEVERE INFANT EPILEPSY
- 61 PEDIATRIC CANCERS DIFFER FROM ADULT CANCERS AND NEED DIFFERENT TREATMENT PLANS

- 62 NEW STEM CELL FOUND IN LUNG, MAY OFFER TARGET FOR REGENERATIVE MEDICINE
 - 63 NARROW-SPECTRUM ANTIBIOTICS PERFORMED EQUALLY WELL OR BETTER THAN BROAD-SPECTRUM ONES
 - 64 BIOMARKERS, CLUES TO POSSIBLE THERAPY FOUND IN NOVEL CHILDHOOD NEUROGENETIC DISEASE
-



INGESTING HONEY AFTER SWALLOWING BUTTON BATTERY REDUCES INJURY AND IMPROVES OUTCOMES

THE FINDING

A team of ear, nose, and throat specialists has demonstrated that eating honey after swallowing a button battery has the potential to reduce serious injuries in small children. The research suggests that this common household product may significantly reduce morbidity and mortality from highly caustic batteries.

WHY IT MATTERS

“Button batteries are ingested by children more than 2,500 times a year in the United States, with more than a 12-fold increase in fatal outcomes in the last decade compared to the prior decade,” said Ian N. Jacobs, MD, director of the Center for Pediatric Airway Disorders and a pediatric otolaryngologist at Children’s Hospital of Philadelphia. “Since serious damage can occur within two hours of ingesting a battery, the interval between ingestion and removal is a critical time to act in order to reduce esophageal injury.”

WHY IT MATTERS

“Button batteries are ingested by children more than 2,500 times a year in the United States, with more than a 12-fold increase in fatal outcomes in the last decade compared to the prior decade,” said [Ian N. Jacobs, MD](#), director of the [Center for Pediatric Airway Disorders](#) and a pediatric otolaryngologist at Children’s Hospital of Philadelphia. “Since serious damage can occur within two hours of ingesting a battery, the interval between ingestion and removal is a critical time to act in order to reduce esophageal injury.”

WHO CONDUCTED THE STUDY

Co-principal investigators Dr. Jacobs and Kris R. Jatana, MD, a pediatric otolaryngologist and director of Pediatric Otolaryngology Quality Improvement at Nationwide Children’s Hospital, led the study.

HOW THEY DID IT

To determine successful interventions for mitigating these injuries in both home and clinical settings, researchers worked with animal models to test the effectiveness of palatable, viscous liquids that could create a protective barrier between the tissue and the battery, as well as neutralize harsh alkaline levels. The researchers screened various options, including juices, sodas, and sports drinks.

“We explored a variety of common household and medicinal liquid options, and our study showed that honey and sucralfate demonstrated the most protective effects against button battery injury, making the injuries more localized and superficial,” Dr. Jacobs said.

QUICK THOUGHTS

“Our recommendation would be for parents and caregivers to give honey at regular intervals before a child is able to reach a hospital, while clinicians in a hospital setting can use sucralfate before removing the battery,” Dr. Jacobs said. However, the authors caution against using these substances in children who have a clinical suspicion of existing sepsis or perforation of the esophagus, known severe allergy to honey or sucralfate, or in children less than 1-year-old due to a small risk of botulism.

WHAT’S NEXT

The study’s findings will be put immediately into clinical practice by incorporating them into the latest National Capital Poison Center Guidelines for management of button battery ingestions.

WHERE THE STUDY WAS PUBLISHED

The study was [published online by *The Laryngoscope*](#).

WHO HELPED FUND THE STUDY

Funding support came from CHOP’s Frontier Program Grant.

WHERE TO LEARN MORE

You can learn more about this research by reading a [press release by CHOP’s Center for Pediatric Airway Disorders](#).

CHILDREN WITH CURRENT ALLERGIES SHOULD BE SCREENED FOR A CHRONIC FOOD ALLERGY



THE FINDING

A research team led by allergists at Children's Hospital of Philadelphia discovered that children were nine times more likely to develop an emerging, chronic food allergy called [eosinophilic esophagitis \(EoE\)](#) if they had three allergies other than EoE, as compared with children with no pre-existing allergies. Children with EoE, a painful inflammation of the esophagus also had a higher risk than those without EoE of developing the respiratory allergy [allergic rhinitis](#) — commonly referred to as seasonal allergy.

WHY IT MATTERS

The study is the first to suggest that EoE was a component of the “allergic march,” a pillar concept in the allergy field, which is usually compressed into the first five years of life. The typical childhood progression is a skin allergy, such as atopic dermatitis, followed by an anaphylactic food allergy, then a respiratory allergy, such as asthma. However, a key implication of the current study is that primary care clinicians should incorporate early EoE screening in children who have other allergies.

WHO CONDUCTED THE STUDY

[David A. Hill, MD, PhD](#), an allergist at CHOP, and [Jonathan M. Spergel, MD, PhD](#), who leads the hospital's [Food Allergy Center](#), led the study.

HOW THEY DID IT

The researchers analyzed health records of more than 130,000 patients in the CHOP pediatric network who were followed from birth to adolescence to determine whether and when patients acquired allergic diseases. The researchers also compared the risk of developing EoE between allergic and non-allergic children.

QUICK THOUGHTS

“The more allergies a child has, the higher is that child's risk of developing EoE,” Dr. Hill said. “The connection among these allergies suggests a common underlying genetic or biological cause, and also may imply that if we can successfully treat an earlier type of allergy, we may prevent later allergies.”

WHAT'S NEXT

The next step is to further investigate the underlying biological mechanisms among different allergies. “Ultimately, we hope to find that intervening earlier in the allergic march, for example, in treating allergic skin conditions, may interrupt the march and prevent the child from developing later disorders such as EoE,” Dr. Hill said.

WHERE THE STUDY WAS PUBLISHED

The study was published online by the [Journal of Allergy and Clinical Immunology: In Practice](#).

WHO HELPED FUND THE STUDY

Grants from the National Institutes of Health, the Food Allergy Research & Education Inc. Clinical Network, and the Consortium of Eosinophilic Gastrointestinal Disease Researchers supported this research.

WHERE TO LEARN MORE

You can learn more about this research by reading a [Cornerstone post](#).



ORAL ANTIBIOTICS MAY RAISE RISK OF KIDNEY STONES

THE FINDING

Children and adults treated with some oral antibiotics have a significantly higher risk of developing kidney stones, according to new research. This is the first time that these medicines have been linked to this condition, with the strongest risks appearing at younger ages and among patients most recently exposed to antibiotics.

Researchers found that five classes of oral antibiotics were associated with a diagnosis of kidney stone disease: oral sulfas, cephalosporins, fluoroquinolones, nitrofurantoin, and broad-spectrum penicillins. They also discovered that patients who received sulfa drugs were more than twice as likely as those not exposed to sulfa drugs to have kidney stones. For broad-spectrum penicillins, the increased risk was 27 percent higher.

WHY IT MATTERS

“The overall prevalence of kidney stones has risen by 70 percent over the past 30 years, with particularly sharp increases among adolescents and young women,” said study leader [Gregory Tasian, MD, MSCE](#), a [pediatric urologist](#) at Children’s Hospital of Philadelphia. Dr. Tasian noted that kidney stones were previously rare in children.

Study co-author [Michelle Denburg, MD, MSCE](#), a [pediatric nephrologist](#) at CHOP, added, “The reasons for the increase are unknown, but our findings suggest that oral antibiotics play a role, especially given that children are prescribed antibiotics at higher rates than adults.”

WHO CONDUCTED THE STUDY

Drs. Tasian and Denburg led the study and co-authored the paper with [Jeffrey Gerber, MD, PhD](#), an infectious diseases specialist at CHOP who leads programs in [antibiotic stewardship](#), and [Lawrence Copelovitch, MD](#), a pediatric nephrologist who co-directs the Kidney Stone Center at CHOP with Dr. Tasian.

HOW THEY DID IT

The study team drew on an electronic health records database from the United Kingdom available through the Center for Clinical Epidemiology and Biostatistics in the [Perelman School of Medicine](#) at the [University of Pennsylvania](#). This database included over 13 million people (adults and children) seen by general practitioners between 1994 and 2015. The team analyzed prior antibiotic exposure for nearly 26,000 patients with kidney stones, compared to nearly 260,000 control subjects.

QUICK THOUGHTS

“Our findings suggest that antibiotic prescription practices represent a modifiable risk factor — a change in prescribing patterns might decrease the current epidemic of kidney stones in children,” Dr. Tasian said. In fact, approximately 30 percent of antibiotics prescribed in office visits are inappropriate, and children receive more antibiotics than any other age group, so the new findings reinforce the need for clinicians to be careful in prescribing correct antibiotics, he pointed out.

WHAT'S NEXT

The researchers are continuing to investigate the microbiomes of children and adolescents with kidney stones at CHOP. They plan to expand their research to better understand how variations in microbiome compositions may influence the development of kidney stones.

WHERE THE STUDY WAS PUBLISHED

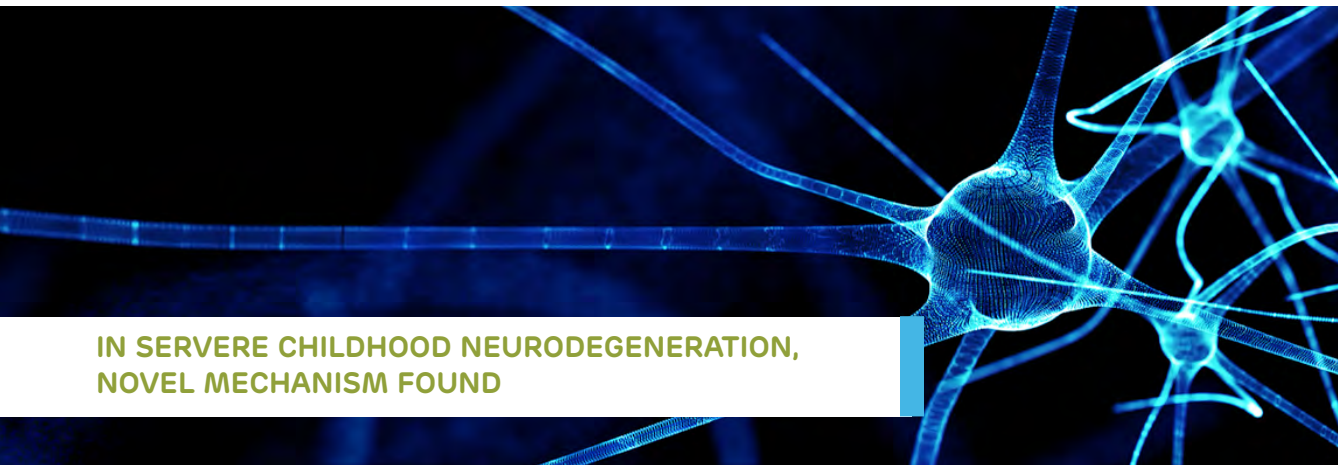
The study was published online by the [Journal of the American Society of Nephrology](#).

WHO HELPED FUND THE STUDY

Grants from the National Institutes of Health supported this research.

WHERE TO LEARN MORE

You can learn more about this research by reading a [press release by CHOP’s Pediatric Kidney Stone Center](#).



IN SEVERE CHILDHOOD NEURODEGENERATION, NOVEL MECHANISM FOUND

THE FINDING

Researchers have discovered gene mutations that severely disrupt crucial functions in mitochondria, the energy-producing structures within cells, are behind a rare but devastating neurological regression in infants. Mutations in the gene PMPCB interfere with the function of the enzyme mitochondrial processing protease (MPP), which cleaves mitochondrial proteins in order to activate these proteins as part of normal biological processing.

It turns out that disrupting that process blocked the production of iron-sulfur clusters that are crucial to energy metabolism and other cellular functions. In infants, diminished MPP activity leads to a potentially catastrophic biological energy deficiency.

WHY IT MATTERS

The disease mechanism, in which mutations disrupt a critical mitochondrial enzyme, has not previously been implicated in humans. The discovery offers new hope for a cure. “If we better understand biological pathways and mechanisms, we may be able to start screening for compounds that may suggest potential treatments for this condition,” said [Ingo Helbig, MD](#), a pediatric neurologist at Children’s Hospital of Philadelphia.

WHO CONDUCTED THE STUDY

Dr. Helbig, who discovered the role of the gene in human disease and who served as the lead investigator, collaborated with researchers from Germany, Australia, and the U.S. on the study.

HOW THEY DID IT

Researchers studied the DNA of five affected children in four families, including three affected children who died before age 6. The research team used whole-exome sequencing to pinpoint the causative mutations in the gene PMPCB. Because that gene is highly conserved across yeast and humans, the researchers then conducted experiments in yeast to investigate the effects of the mutation.

QUICK THOUGHTS

“We uncovered the cause of this mysterious neurodegenerative disease, and now we understand better what happens in the brains of these children,” Dr. Helbig said. “This new understanding is the very first step toward potentially finding a treatment.”

WHAT’S NEXT

The current findings set the stage for follow-up research in biological implications, for instance, by further investigation in yeast models of the disease. “We realized that that the disease mechanisms of this condition can be reliably modeled in yeast,” Dr. Heilbig said. “We can therefore use this model to assess for ways to modify the disease process in order to find treatments.”

WHERE THE STUDY WAS PUBLISHED

The study was published online by the [American Journal of Human Genetics](#).

WHO HELPED FUND THE STUDY

Multiple sources contributed funding support, including the German Research Foundation, the University of Kiel, the German Research Foundation (Deutsche Forschungsgemeinschaft), the Japan Agency for Medical Research and Development, Miracles for Mito, Summits for Samantha, and the Children’s Hospital Colorado Foundation.

WHERE TO LEARN MORE

You can learn more about this research by reading a [press release by the Division of Neurology](#). Dr. Helbig also introduced this finding on this research blog [“Beyond the Ion Channel.”](#)



TARGETING A BRAIN CIRCUIT LED TO 'ANTIDEPRESSIVE' BEHAVIOR IN ANIMAL MODELS

THE FINDING

Researchers identified a pathway in brain circuitry that, when stimulated, leads to “antidepressive” behavior in animal models. If such brain stimulation proves to have similar effects in people, it may eventually lead to a novel treatment for depression.

WHY IT MATTERS

“Our group was the first to investigate whether stimulating Ent (the entorhinal cortex) could affect mood,” according to Sanghee Yun, PhD, research assistant professor of Anesthesiology and Critical Care at Children’s Hospital of Philadelphia. “Our findings are the first evidence that targeting this particular brain circuit may offer a potential new depression treatment.”

WHO CONDUCTED THE STUDY

[Amelia Eisch, PhD](#), a neurobiology researcher, led the study, and Dr. Yun was the paper’s first author. Both are from the [Department of Anesthesiology and Critical Care](#) at CHOP.

HOW THEY DID IT

Researchers worked with a mouse model genetically engineered to “knock down” or eliminate a previously identified protein called TRIP8b, which increases during stress and inhibits cell firing. The researchers stimulated a region upstream from the brain’s hippocampus, the entorhinal cortex (Ent). The mice with greater stimulation in their Ent circuits showed antidepressive behaviors.

QUICK THOUGHTS

“Major depressive disorder is a serious health problem worldwide. Existing treatments are helpful for many people, but also have a high rate of relapse and significant side effects,” Dr. Eisch said. “Because scientists consider depression to be caused by malfunctions in brain circuitry, we suggest that ‘tuning’ a specific circuit could set the stage for a targeted treatment.”

WHAT’S NEXT

The researchers hope the study findings present opportunities to collaborate with translational researchers to pursue promising implications for practical, noninvasive treatments for people with depression.

“Existing brain stimulation therapies for depression are extremely helpful for many patients, but they don’t work for everyone, and they also have side effects such as memory loss and cognitive impairment,” Dr. Eisch said. “It is important to increase the number of tools available to treat depression and find those with fewer side effects as well.”

WHERE THE STUDY WAS PUBLISHED

The study was published online by [Nature Medicine](#).

WHO HELPED FUND THE STUDY

Grants from the National Institutes of Health, the National Aeronautics and Space Administration, and the National Alliance for Research on Schizophrenia and Depression supported the study.

WHERE TO LEARN MORE

You can learn more about this research by reading a [press release by CHOP’s Department of Anesthesiology and Critical Care Medicine](#).



IN HUNTINGTON'S DISEASE, HEART PROBLEMS SHED LIGHT ON DISEASE PROGRESS

THE FINDING

Researchers investigating a key signaling protein in Huntington's disease (HD), an incurable, inherited disease with progressive loss of brain cells and motor function, discovered deleterious effects on heart function beyond the rare disease's devastating neurological impact.

A defective gene produces repeated copies of a protein called huntingtin, or HTT. The mutant HTT protein (mHTT) causes involuntary movements and severe cognitive and emotional disturbances. The study found that adjusting the protein levels improved heart function in mice with HD.

WHY IT MATTERS

"Heart disease is the second leading cause of death in Huntington's disease patients, but its biology remains poorly understood," said [Beverly Davidson, PhD](#), director of the [Raymond G. Perelman Center for Cellular and Molecular Therapeutics](#) at Children's Hospital of Philadelphia, where she is an expert on gene therapy for inherited brain disorders. "Better knowledge of the underlying biology of Huntington's disease will improve the development of effective therapies."

About 30,000 Americans have HD.

WHO CONDUCTED THE STUDY

Dr. Davidson led the study team.

HOW THEY DID IT

The study focused on heart function in mice with HD. The mutant protein mHTT disrupts functioning along the mTORC1 pathway, named for the signaling protein complex mTORC1 that promotes cellular growth and metabolism and plays a key role in the neurology of HD.

Researchers found mTORC1 activity was lower in HD mice than in healthy mice and that the HD mice also had smaller-than-normal hearts. The study team discovered that HD mice were less able to adapt to stress on their hearts and had higher mortality from that stress. However, when the researchers restored mTORC1 activation in the HD mice by using genetic techniques to knock down the mutant HTT protein, the mice were better able to adapt to cardiac stress and had higher survival over the course of the study.

QUICK THOUGHTS

"We know from [our previous studies](#) that improving mTORC1 functioning may have a protective effect in HD, but this would require carefully adjusting the pathway to restore normal mTORC1 levels," Dr. Davidson said. The new study suggests that improving mTOR function in hearts would also be beneficial.

WHAT'S NEXT

The researchers hope that future studies will investigate whether the mHTT protein has a similar effect on human hearts as in the mice, which may help explain the heart-related mortality seen in patients with HD.

WHERE THE STUDY WAS PUBLISHED

The study was published online in [Cell Reports](#).

WHO HELPED FUND THE STUDY

Several grants from the National Institutes of Health supported the study.

WHERE TO LEARN MORE

You can learn more by reading a [press release by CHOP's Division of Neurology](#).



TEEN DRIVERS WITH ADHD SYMPTOMS HAVE MORE RISKY DRIVING BEHAVIORS

THE FINDING

New research shows drivers with [attention-deficit/hyperactivity disorder](#) (ADHD) symptoms are more likely to be involved in a crash. In fact, researchers found the more inattention symptoms a teen reported, the more mistakes they made in a driving simulator.

WHY IT MATTERS

Teenage drivers ages 16 to 19 are three times more likely to get into fatal accidents than their older counterparts. Approximately 20 percent of U.S. teens in this age group have been affected by symptoms associated with mental health disorders, including 9 percent with a lifetime history of ADHD. This study seeks to shed light on the relationship between these findings.

WHO CONDUCTED THE STUDY

[Catherine McDonald, PhD, RN, FAAN](#), a senior fellow at Children's Hospital of Philadelphia's [Center for Injury Research and Prevention \(CIRP\)](#) and assistant professor in the Department of Family and Community Health at the [University of Pennsylvania School of Nursing](#), led the research study.

HOW THEY DID IT

The research team recruited drivers aged 16 to 17 years old and asked them to complete a questionnaire that assessed their symptoms of ADHD and other mental health disorders. The teens were then asked to go for a virtual drive in the [CIRP Driving Simulator Core](#) to assess their driving skills.

QUICK THOUGHTS

"Previous studies have shown increases in crash-risk related to an ADHD diagnosis," Dr. McDonald said. "We wanted to tease apart the nuances behind that. Is it about risk-taking, skill, or performance deficits? Is it about decision-making? In the capacity of a simulator as well as self-reported behaviors, we wanted to see if our data could get at the why of what is happening around driving behaviors."

WHAT'S NEXT

"We would like to learn more about the relationship of mental health symptoms to driving behavior in a sample with higher rates and severity of ADHD so we can examine the impact of inattention and hyperactivity-impulsivity symptom severity across the full range of these dimensions," Dr. McDonald said. That next step could move the research toward its ultimate goal: tailoring interventions for teen drivers at risk in different ways.

Where the study was published: The findings were published online in the journal [Nursing Research](#).

WHO HELPED FUND THE STUDY

Grants from the National Institutes of Health and Penn Nursing's Dorothy Mereness Endowed Research Fund supported the research study.

WHERE TO LEARN MORE

You can learn more by reading [CIRP's Research in Action post](#).



MISSING MUTATION' FOUND IN SEVERE INFANT EPILEPSY

THE FINDING

Researchers discovered a “missing mutation” in severe infant epilepsy that leads to epileptic seizures. They also found early indications that specific medications might prevent disabling brain injury by controlling epilepsy during a crucial period shortly after birth.

WHY IT MATTERS

“These are still early days, but we may be able to use this knowledge to protect the newborn brain and improve a child’s long-term outcome,” said [Ethan Goldberg, MD, PhD](#), a pediatric neurologist at Children’s Hospital of Philadelphia.

The study focused on mutations in the gene SCN3A, which had been previously linked to less severe forms of epilepsy but had not clearly been proven to be an epilepsy gene. SCN3A encodes the sodium channel Nav1.3 which regulates electrical activity in neurons of the developing brain. The current research solidified this link and was the first to establish that SCN3A mutations cause the severe infantile form, known as epileptic encephalopathy. Researchers also found that existing anti-seizure medications — lacosamide and phenytoin — could help treat this condition.

WHO CONDUCTED THE STUDY

Dr. Goldberg along with [Ingo Helbig, MD](#), physician in the Division of Neurology, led the study team of European and American researchers, including several from CHOP.

HOW THEY DID IT

The researchers reported on a cohort of four unrelated children from different countries, all of whom had severe epilepsy with a particularly early onset that did not respond to medication and resulted in expected lifelong disability. The researchers used whole-exome sequencing to pinpoint mutations in the SCN3A gene, which were present in the affected children, but not inherited from their parents. Cell studies further revealed detailed properties of the electrical signaling process.

QUICK THOUGHTS

Precise, early diagnosis may be crucial because of the highly regulated timetable of early-life neurological events. “The mutation’s activity in the Nav1.3 sodium ion channel occurs during a short period in newborns, but if we can intervene during that window, we may be able to help prevent long-term neurological injury and benefit patients,” Dr. Goldberg said.

WHAT’S NEXT

Further research in stem cell-derived neurons from patients with SCN3A encephalopathy and in animal models will be necessary to test possible precision-medicine treatments for safety and efficacy before they can be investigated in patients. Dr. Goldberg’s team is actively pursuing these leads. Drs. Goldberg and Helbig have a growing cohort of more than 20 patients with SCN3A encephalopathy who have been identified since the initial publication.

The current research has resulted in the addition of the SCN3A gene to an existing diagnostic test, CHOP’s Epilepsy Panel, which uses next-generation sequencing to rapidly test for more than 100 genetic causes of childhood epilepsy.

WHERE THE STUDY WAS PUBLISHED

The study was published online by the [Annals of Neurology](#).

WHO HELPED FUND THE STUDY

The National Institutes of Health and the Burroughs Wellcome Fund Career Award for Medical Scientists provided funding for this study.

WHERE TO LEARN MORE

You can learn more about this research by reading a [press release by CHOP’s Pediatric Epilepsy Program](#) and on [Dr. Helbig’s blog](#).



PEDIATRIC CANCERS DIFFER FROM ADULT CANCERS AND NEED DIFFERENT TREATMENT PLANS

THE FINDING

Researchers found important differences in how cancers develop in children compared to how they develop in adults. For instance, they identified 142 genes that drive pediatric cancers, but only 45 percent of those genes match genes found in adult pan-cancer studies. This implies that precise treatments need to be better customized for children.

WHY IT MATTERS

Physician-scientists from Children's Hospital of Philadelphia contributed crucial data and expertise to the first pan-cancer analysis of children's cancer. Pan-cancer analyses identify similarities and differences among the biological changes across diverse types of cancer to discover insights for improved care.

WHO CONDUCTED THE STUDY

Jinghui Zhang, PhD, of St. Jude Children's Research Hospital, led the study team. Co-authors of the study from CHOP lead the two largest datasets in the study: [Stephen Hunger, MD](#), CHOP's chief of Oncology, leads the TARGET team for acute lymphoblastic leukemia, and [John M. Maris, MD](#), leads the neuroblastoma TARGET team. [Sharon Diskin, PhD](#), a faculty member of the Division of Oncology and the [Center for Childhood Cancer Research](#) at CHOP, was also an author of the study.

HOW THEY DID IT

The researchers analyzed DNA samples from nearly 1,700 patients from multiple centers across five groups of pediatric cancers: acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), neuroblastoma, Wilms' tumor and osteosarcoma.

QUICK THOUGHTS

"As pediatric centers have developed precision medicine strategies, many have relied on diagnostic panels developed to detect mutations common in adult cancers. In contrast, CHOP has developed diagnostic panels specific to mutations common in pediatric cancers — many of which occur only rarely in adult cancers," Dr. Hunger said.

WHAT'S NEXT

"This collaborative project proves the concept that childhood cancers are not 'small adult tumors.' They show unique genetic changes. Thus, precision diagnostic and therapeutic strategies for childhood cancers will be very different than those being developed for common adult malignancies," Dr. Maris said.

WHERE THE STUDY WAS PUBLISHED

The study was published online and in print by the journal [Nature](#).

WHO HELPED FUND THE STUDY

Patients were in clinical trials sponsored by the Children's Oncology Group.

WHERE TO LEARN MORE

You can learn more about this research by reading a [press release by CHOP's Cancer Center](#).



NEW STEM CELL FOUND IN LUNG, MAY OFFER TARGET FOR REGENERATIVE MEDICINE

THE FINDING

A study team identified a new cell lineage, which they called alveolar epithelial progenitor (AEP) cells. Researchers focused on the alveoli — tiny compartments in the lung in which gas exchange occurs — as oxygen is taken up by the blood and carbon dioxide is removed. They discovered that certain powerful stem cell signaling pathways act on AEP cells in the lung to orchestrate their response to injury. Activated AEP cells multiply rapidly and differentiate into alveolar cells, thereby regenerating lung tissue.

WHY IT MATTERS

The discovery could provide an opportunity to develop innovative future treatments that harness the body's ability to regenerate. AEP cells could be used to treat lung diseases in individuals of all ages, from premature infants to the elderly.

WHO CONDUCTED THE STUDY

[Edward Morrissey, PhD](#), director of the Penn Center for Pulmonary Biology and Scientific Director of Penn's Institute for Regenerative Medicine, led the research team, and [David Frank, MD, PhD](#), a pediatric cardiologist at Children's Hospital of Philadelphia, was the study's co-first author.

HOW THEY DID IT

The researchers studied a mouse model of lung injury caused by influenza virus. The researchers found that AEP cells share similar characteristics in both mice and humans, which allowed them to perform experiments in organoid models — three-dimensional cell cultures that simulated specific ways that lungs regenerate in living lower organisms.

QUICK THOUGHTS

"These cells sit quietly, but poised, in the lung until an injury activates them to proliferate and differentiate," Dr. Frank said. "If we can learn to manipulate the biological signals in this process, we may be able to regenerate lung tissue in patients."

WHAT'S NEXT

The researchers hope to translate their findings into eventual treatments for lung diseases such as bronchopulmonary dysplasia, a severe, sometimes fatal disability in infants with underdeveloped lungs; chronic obstructive pulmonary disease in adults; and severe lung damage from influenza in individuals of any age. The findings might even play a part in developing future tissue engineering treatments for premature babies or patients needing lung transplantation.

WHERE THE STUDY WAS PUBLISHED

The study was published online in the journal [Nature](#).

WHO HELPED FUND THE STUDY

Several grants from the National Institutes of Health supported this study.

WHERE TO LEARN MORE

You can learn more about this research by reading a [press release by CHOP's Pulmonary Hypertension Program](#).



NARROW-SPECTRUM ANTIBIOTICS PERFORMED EQUALLY WELL OR BETTER THAN BROAD-SPECTRUM ONES

THE FINDING

Researchers found that, when judged by both practical and clinical outcomes, narrow-spectrum antibiotics performed just as well or better than broad-spectrum ones, and result in fewer disruptions to family routines, such as adverse drug effects and missed school days.

In treating earaches, strep throat, and other common infections, researchers discovered a significantly higher risk of adverse events for broad-spectrum antibiotics compared to narrow-spectrum antibiotics (3.7 percent vs. 2.7 percent as documented by clinicians, and 35.6 percent vs. 25.1 percent, as reported by patients and families). However, the rates of treatment failure were not significantly different between both types of antibiotics.

WHY IT MATTERS

The study reflects an “antimicrobial stewardship” approach, guiding healthcare providers to prescribe the most appropriate antibiotic for a patient’s specific type of infection, with the aim of improving individual outcomes and reducing the overall risk of antibiotic resistance — in which disease-causing microorganisms develop resistance to commonly used antibiotics.

“Many children unnecessarily receive broad-spectrum antibiotics for common infections, which can lead to antibiotic resistance and unnecessary side effects,” said study leader [Jeffrey Gerber, MD, PhD](#), associate director for Inpatient Research Activities in the [Center for Pediatric Clinical Effectiveness \(CPCE\)](#) at Children’s Hospital of Philadelphia. “This study showed that inappropriate prescribing of antibiotics also affects families at a much more practical level, such as missed days from school and work, side effects of the drugs, and costs for extra childcare. These can be a real burden for families.”

WHO CONDUCTED THE STUDY

Dr. Gerber led the study.

HOW THEY DID IT

The study team performed two complementary studies in 31 primary care practices in CHOP’s pediatric network in Pennsylvania and New Jersey, between January 2015 and April 2016. They drew on electronic health records of infants and children up to age 12, who were diagnosed with an acute respiratory tract

infection (ARTI) and prescribed an oral antibiotic. In a retrospective cohort of approximately 30,000 patients, 14 percent received broad-spectrum drugs, and 86 percent received narrow-spectrum drugs. In a prospective cohort of 2,472 children, researchers conducted telephone interviews with caregivers to measure outcomes that parents had identified as their highest concerns: adverse drug effects, additional childcare costs, lingering symptoms, and missed school days.

The ARTIs in the analysis were acute otitis media (earache), Group A streptococcal pharyngitis (strep throat) and sinusitis (sinus infection), which account for the majority of antibiotic exposures in children.

QUICK THOUGHTS

“Research tells us that antibiotic stewardship programs not only reduce the overall burden of antibiotic resistance, but also improve patient outcomes,” Dr. Gerber said. “Our previous research has also shown that these programs can lower costs for insurers and families that pay for prescriptions. These programs are a win-win-win for public health, families, and insurers.”

WHAT’S NEXT

Researchers will use the study findings to build on CHOP’s seven years of research to continuing developing an effective clinical practice model for antibiotic stewardship in pediatric outpatient settings.

WHERE THE STUDY WAS PUBLISHED

The study was published online in the [Journal of the American Medical Association](#).

WHO HELPED FUND THE STUDY

An award from the Patient-Centered Outcomes Research Institute funded the study.

WHERE TO LEARN MORE

You can learn more about this research by reading [a press release by CPCE](#).



**BIOMARKERS, CLUES TO POSSIBLE THERAPY FOUND
IN NOVEL CHILDHOOD NEUROGENETIC DISEASE**

THE FINDING

Researchers studying a rare genetic disorder that causes severe, progressive neurological problems in childhood have discovered new insights into the biological mechanisms that drive the disease. TBCK-encephaloneuropathy (TBCKE) is caused by a mutation in the TBCK gene. TBCKE results in progressive neurodegeneration involving the brain as well as progressive muscle weakness.

The researchers found that abnormalities in a biological waste-disposal process called autophagy links the mechanisms underlying rare pediatric neurogenetic disorders including TBCKE to more common neurodegenerative disorders, such as Huntington’s or Parkinson’s disease. They also discovered that an amino acid supplement might offer a targeted therapy.

WHY IT MATTERS

Scientists already knew that the TBCK protein regulates signals along a biological pathway known as mTOR. Abnormal mTOR signaling has been linked to epilepsy, autism, intellectual disability, and other neurological conditions. A key role for mTOR signaling is in autophagy, the normal cleanup process in which cells dispose of damaged proteins, lipids, and other biological objects. When autophagy doesn’t function normally, neurodegenerative diseases may result.

Researchers in the current study found that a specific mutation on the TBCK gene, called the Boricua mutation, leads to abnormal autophagy. Patients with this mutation are usually of Puerto Rican (Boricua) descent. They also found a potential biomarker for TBCKE — abnormal levels of chemicals called oligosaccharides in the patients’ urine.

Oligosaccharide levels improved when the researchers added the amino acid leucine to the patients’ cells in laboratory cultures.

WHO CONDUCTED THE STUDY

[Xilma R. Ortiz-Gonzalez, MD, PhD](#), a pediatric neurogeneticist at Children’s Hospital of Philadelphia, led the study.

HOW THEY DID IT

The researchers studied a cohort of eight unrelated boys, ranging from age 9 to 14 years, all of Puerto Rican descent. All had the Boricua mutation at the same location on the TBCK gene. They all share a very severe presentation of the disease, including profound intellectual disability, epilepsy, low muscle tone, and progressive dysfunction in both the central and peripheral nervous systems.

QUICK THOUGHTS

“Leucine activates mTOR signaling that was disrupted by the mutation, so this finding suggests that leucine might offer some improvement in disease symptoms if used in patients,” Ortiz-Gonzalez said. This is consistent with [previous CHOP research in a TBCK-related disease](#), which showed potential therapeutic benefits in using leucine in affected cells.

WHAT’S NEXT

Dr. Ortiz-Gonzalez and her CHOP collaborators are continuing to investigate the biology of TBCKE, while working to establish a patient registry of children with the rare disorder. Her goal is to identify more patients and perform studies that could set the stage for a clinical trial to test leucine or a similar compound as a personalized treatment for this severe childhood disease.

WHERE THE STUDY WAS PUBLISHED

The study was published online by the [Annals of Neurology](#).

WHO HELPED FUND THE STUDY

The Robert Wood Johnson Harold Amos Faculty Development Award and several grants from the National Institutes of Health funded the research.

WHERE TO LEARN MORE

You can learn more by reading [a press release by CHOP’s Division of Neurology](#). You can also learn more about Dr. Ortiz-Gonzalez’ research by visiting her [CHOP Research profile](#).

INSPIRATION



66 FOOD ALLERGY FRONTIER PROGRAM SEEKS ANSWERS TO PUZZLING AND EVER-PREVALENT EoE



FOOD ALLERGY FRONTIER PROGRAM SEEKS ANSWERS TO PUZZLING AND EVER-PREVALENT EoE

Born just 13 months apart, 16-year-old brothers Dean and Cole Harris have shared a lot over the years, from the same group of friends to similar hobbies. But the Harris boys, as they're often known by their peers, have something else in common, for better or worse: [eosinophilic esophagitis](#) (EoE), a rare allergic inflammatory disease of the esophagus, or the muscular tube that carries food from the throat to the stomach.

EoE has a strong genetic component, and thus it's not uncommon that when one sibling has the disease, another could have the same condition. For Dean and Cole, dealing with the same digestive disorder has had its blessings. The brothers grew up fiercely supportive of each other, enduring its myriad challenges together.

"In so many ways, they needed each other," said the boys' mom, Suzanne Harris.

In EoE, certain food allergens trigger a congregation of cells in the esophagus, particularly large amounts of white blood cells called eosinophils. This results in a host of adverse reactions, such as vomiting, abdominal pain, heartburn sensations, and failure to thrive. Unlike [classic food allergies](#), simply eliminating the suspect allergen from one's diet is difficult. Those with EoE can be sensitive to a number of foods, and clinicians currently cannot predict which foods trigger a reaction.

Thanks to great progress in clinical and lab research, researchers have a clearer picture of EoE pathogenesis than they did 30 years ago, when the condition was virtually unknown. But [Jonathan Spergel, MD, PhD](#), chief of the Division of Allergy at Children's Hospital of Philadelphia, believes that our understanding of EoE, a puzzling and increasingly prevalent disease, is far from complete.

Clinicians still lack a noninvasive method to monitor the disease and to identify trigger foods for each patient. There are currently no approved medications to treat EoE, though doctors have had success approaching EoE with a managed diet and a topical steroid to control its symptoms. Furthermore, one big question remains: Why do some children — including Dean and Cole — end up outgrowing the disease, which was previously considered a lifelong, incurable condition? With new fuel as a designated 2018 Frontier Program at CHOP, Dr. Spergel believes his team can continue to discover more about EoE and improve the quality of life for children and adolescents like Dean and Cole around the world.

GROWING UP WITH EOE: DEAN AND COLE'S STORY

As infants, both Dean and Cole had problems taking in the food and nutrients they needed to thrive: As Suzanne tried to nurse baby Dean, he began to hemorrhage, leading doctors to suspect he had a milk protein allergy. Meanwhile, to Suzanne, it seemed like Cole was born vomiting, and at 3-weeks-old, he had undergone two surgeries. Doctors guessed he might have the same milk protein allergy as Dean or [pyloric stenosis](#), a thickening of a stomach muscle that can affect how food travels to the intestine. Though Cole tolerated tube-feeding of an amino acid based formula, when he was 4-weeks-old, his heart stopped, leading Suzanne to perform life-saving CPR. She realized Cole had more than just a milk protein allergy.

Over the next few years, the boys spent years in and out of hospitals and emergency rooms, seeing allergists, pulmonologists, gastroenterologists, and other specialists for a host of problems, including compromised immune systems and growth problems due to their difficult breathing and vomiting episodes.

“Nobody knew what was wrong with them,” Suzanne said.

Finally, after a series of tests at Cincinnati Children’s [Aerodigestive and Esophageal Center](#), doctors suggested that the Harris boys might have EoE.

“I felt as though the enemy had a name,” Suzanne said.

After finding out everything she could about EoE and taking the initiative to attend a research conference hosted by the [American Partnership for Eosinophilic Disorders](#) in Cherry Hill, NJ, Suzanne learned that CHOP was one of the only hospitals in the world with a division specifically dedicated to EoE treatment. Within 24 hours, the Harris family had packed up and moved to Ocean City, NJ, to be closer to CHOP’s [Center for Pediatric Eosinophilic Disorders](#).

TREATMENT AT CHOP AND A SURPRISE DISCOVERY

Dean and Cole began a series of food trials at CHOP under the guidance of Dr. Spergel’s team. Since clinicians can only guess what food groups trigger a reaction in patients, they often impose dietary restrictions on patients followed by an endoscopy and a biopsy to try to pinpoint allergens.

The boys loved allergy testing days for two reasons: It gave them the opportunity to taste something new along with the hope that they might learn what triggered their inability to maintain a normal diet. But after testing a variety of foods, clinicians were perplexed. In the first and second grade, Dean and Cole had to stop eating altogether in order to wipe their dietary slates clean, subsisting on a medical amino acid formula while they re-introduced food after food.

By this time, EoE was taking a bigger toll on their school, social lives, and general well-being. Dean wore braces on his legs due to poor bone health. The boys worried about attending social events due to their diets. And Suzanne was trying her best to make family meals fun despite the not-so-fun taste and feel of medical formula.

Finally, Dr. Spergel suggested that Dean might like to participate in the SMILEE study, a trial designed by Dr. Spergel in partnership with the pharmaceutical company, DBV Technologies, to [investigate the effectiveness of a skin patch](#) with novel epicutaneous immunotherapy (EPIT) for treating EoE. The patch is intended to desensitize allergic reactions to dairy by keeping an allergen — in this case milk — on the skin for repeated and prolonged periods. Dean’s decision to participate in the study led to a surprise discovery for Dr. Spergel and a game-changer for Suzanne and the boys.

The study had required that Dean stop taking his medication and begin to consume dairy, which had always made him very sick. For the first time in 13 years, Dean ate a slice of cheese pizza. A few weeks into the study, Suzanne received a call from CHOP. The nurse couldn’t explain it, but Dean’s biopsy had come back clear. Two biopsies later, it was more or less confirmed: Dean had outgrown his EoE. Suzanne remembers her son’s first reaction to the news.

“I picked up Dean from school that day, and I told him, you’re cured. And the first thing he says to me is, what about Cole?”

Hoping that Cole might have also outgrown his EoE, that August, Cole stopped his medication and began to consume foods that he previously could not tolerate. After a scope about three months later, Suzanne received another surprise call from CHOP. Cole’s biopsy, too, showed up completely normal. Almost miraculously, the boys could tolerate foods that had made them very sick for most of their childhood.

“It changed our lives,” Suzanne said. “Dean was the kid with braces on his leg, but when he graduated eighth grade, he was on the wrestling team, the cross-country team, and he was the class president who gave the commencement address. That was not his fate. So, my wish is that clinicians learn more about that differentiating factor in children who get well — knowing those differences has to bring hope to people.”

Dean and Cole are two of Dr. Spergel's small subset of pediatric patients who were discovered to have outgrown their EoE. As described in one of his papers published in the [Journal of Allergy and Clinical Immunology](#) this past year, the discovery forms a key building block in our understanding of the disease. Contrary to existing knowledge, EoE was not a lifelong condition, and with more research, clinicians could very well develop effective treatments.

ACCELERATING EOE RESEARCH: PAST AND FUTURE FINDINGS

Frontier Program funding and support will accelerate the Food Allergy Center's search for a cure and effective ways to monitor the disease. These advances hold the potential to improve the difficult experiences that patients like Dean and Cole endured growing up with EoE. On top of continuing work with DBV Technologies on the SMILEE trial (with results to be published in the near future), food allergy researchers at CHOP are developing a novel blood test that will help clinicians establish better treatment regimens for EoE.

"One of the major difficulties of EoE research is that we have no way to monitor the disease without doing endoscopies and invasive biopsies," Dr. Spergel said. "So one of the goals of the [Frontier program](#) is to develop a noninvasive biomarker to follow the disease without putting patients under anesthesia."

Dr. Spergel's team has already laid much of the groundwork for this research pipeline this past year. In research published in the [Annals of Allergy, Asthma and Immunology](#), a team led by [Antonella Cianferoni, MD, PhD](#), attending physician in the Allergy Section at CHOP, described their development of an assay for T-cells to examine how the cells function in the peripheral blood of patients with EoE; the researchers had discovered that in patients with EoE, T-cells have specific activation to milk allergens.

"With patients with EoE, we've seen T-cells get activated, so the idea is to try to take that to the next step, not just for milk but for other foods like wheat and dairy, and seeing if we can develop a clinically useful test to measure what foods are causing disease," Dr. Spergel said.

In the last decade, EoE has become increasingly recognized in clinical settings. And as awareness grows, clinicians have the opportunity to learn more about the underlying genetics and pathogenesis of the disease. For this reason, Suzanne believes it's important to stay close to CHOP and continue returning to see Dr. Spergel — for both her boys' health, and that of other children who could benefit from what clinicians learn from Dean and Cole's experiences.

"My boys are getting scoped in November (2018) because they're among the first [patients] to be well," Suzanne said. "So are they well forever? We don't know. Some patients who outgrew the disease might not continue following up. But we want to stay plugged in. And my boys are so excited."



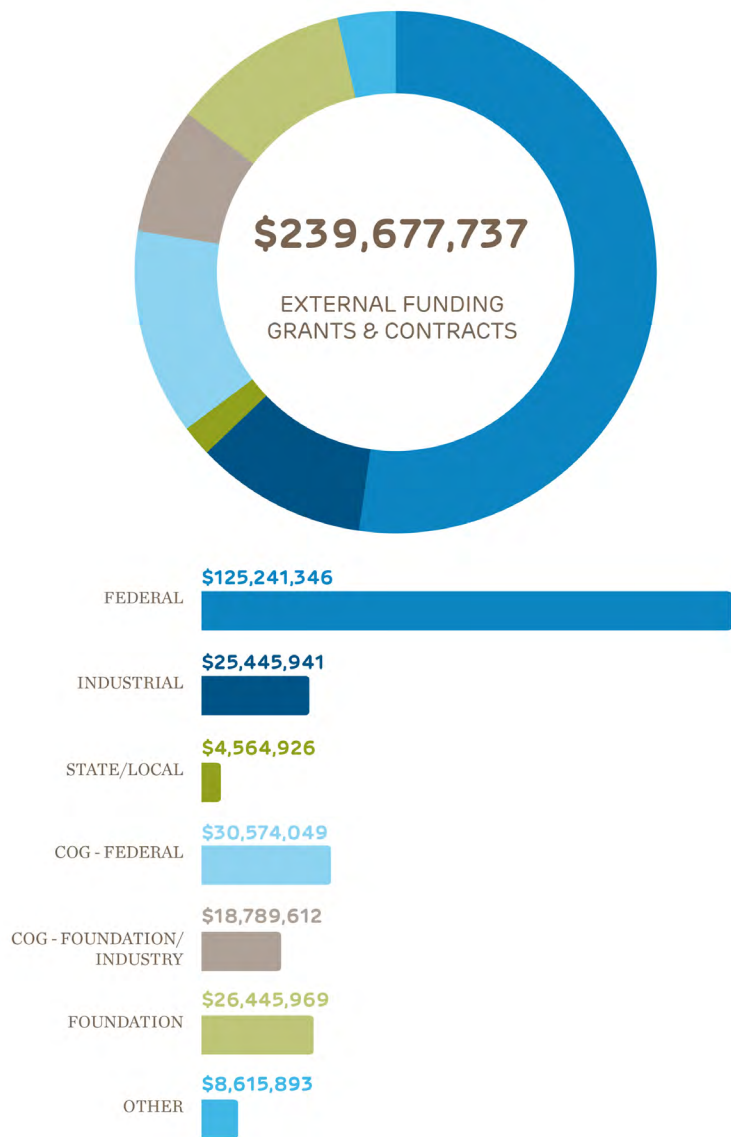
FACTS & FIGURES

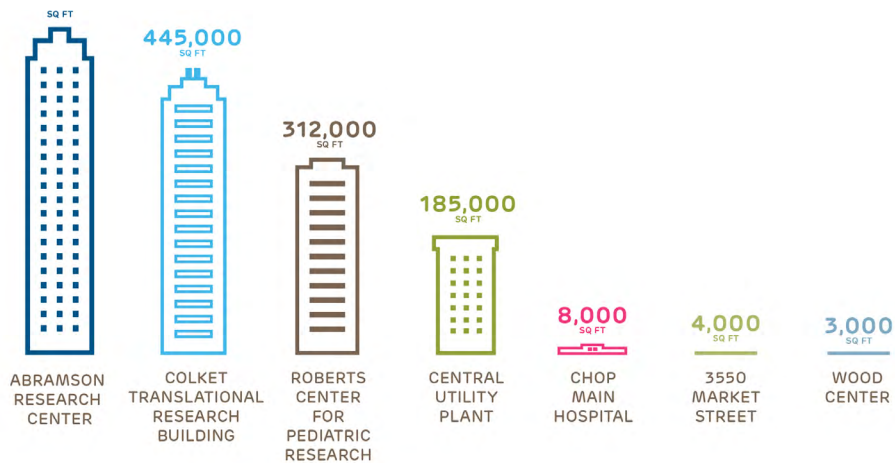
70 FINANCIAL/STATS INFO - FY 18

72 WHO'S WHO - FY 18

84 CREDITS

85 LINKS OF INTEREST





\$416,639,369

TOTAL RESEARCH OPERATING EXPENSES



\$239,677,737

EXTERNAL GRANTS AND CONTRACTS



\$104,799,311

734 AWARDS



2,503

PUBLICATIONS

CHOP RESEARCH INSTITUTE LEADERSHIP

- › **Bryan A. Wolf, MD, PhD**
Chief Scientific Officer & Executive Vice President
- › **Beverly L. Davidson, PhD**
Chief Scientific Strategy Officer
- › **Richard Aplenc, MD, PhD, MSCE**
Assistant Vice President and Chief Clinical Research Officer
- › **Michelle Lewis, MS, CRA**
Vice President, Research Administration and Operations
- › **Zev Sunleaf**
Vice President, Office of Technology Transfer, Commercialization and Innovation
- › **Matthew Hodgson**
Assistant Vice President, Research Compliance and Regulatory Affairs
- › **Jeffrey Pennington**
Associate Vice President and Chief Research Informatics Officer

CENTERS OF EMPHASIS

- › [Center for Applied Genomics](#)
Director: [Hakon Hakonarson, MD, PhD](#)
- › [Center for Autism Research](#)
Director: [Robert Schultz, PhD](#)
- › [Center for Childhood Cancer Research](#)
Director: [Stephen P. Hunger, MD](#)
- › [Center for Computational and Genomic Medicine](#)
Director: [Yi Xing, PhD](#)
- › [Center for Injury Research and Prevention](#)
Directors: [Flaura Winston, MD, PhD](#), and [Kristy Arbogast, PhD](#)

- › [Center for Mitochondrial and Epigenomic Medicine](#)
Director: [Douglas Wallace, PhD](#)
- › [Center for Pediatric Clinical Effectiveness](#)
Director: [Theoklis Zaoutis, MD, MSCE](#)
- › [PolicyLab](#)
Director: [David Rubin, MD, MSCE](#)
- › [Raymond G. Perelman Center for Cellular and Molecular Therapeutics](#)
Director: [Beverly Davidson, PhD](#)

RESEARCH AFFINITY GROUPS

- › **Clinical Trials Research Affinity Group**
Leader: [Pam Weiss, MD, MSC](#)
- › **Developmental Biology**
Leaders: [Judy Grinspan, PhD](#), and [Stewart Anderson, MD](#)
- › **Fetal Biology and Therapy**
Leader: [Alan Flake, MD](#)
- › **Genes, Genomes, and Pediatric Disease**
Leaders: [Yael Mosse, MD](#), and [Marcella Devoto, PhD](#)
- › **Global Health**
Leaders: [Elizabeth Lowenthal, MD, MSCE](#)
- › **Health and Behavior**
Leaders: [Stephen Leff, PhD](#), and [Joel Fein, MD, MPH](#)
- › **Metabolism, Nutrition, and Physical Development**
Leader: [Babette Zemel, PhD](#)
- › **METACHOP (Math, Engineering, Technology)**
Leader: [Helen Loeb, PhD](#)
- › **mHealth**
Leaders: [Nadia Dowshen, MD](#), [Linda Fleisher, PhD](#), and [Lisa Schwartz, PhD](#)
- › **Mitochondria**
Leader: [Marni Falk, MD](#)
- › **Neuroscience**
Leader: [Michael Robinson, PhD](#)
- › **Normal and Malignant Hematopoiesis**
Leader: [Carolyn Felix, MD](#)
- › **Proteins**
Leader: [Yair Argon, PhD](#)
- › **Protective Immunity and Immunopathology**
Leaders: [Edward Behrens, MD](#), and [Paula Oliver, PhD](#)

› **Qualitative Methods**

Leader: [Cynthia Mollen, MD, MSCE](#)

› **Spatial and Functional Genomics**

Leaders: [Struan Grant, PhD](#), [Andrew Wells, PhD](#), and [Gerd Blobel, MD, PhD](#)

› **Stem Cells and Benign Hematopoiesis**

Leaders: [Mortimer Poncz, MD](#) and [Deborah French, PhD](#)

ENDOWED CHAIRS

› **Leonard and Madlyn Abramson Endowed Chair in Pediatrics**

Holder: Joseph W. St. Geme III, MD

› **Leonard and Madlyn Abramson Endowed Chair in Pediatric Urology**

Holder: Douglas A. Canning, MD

› **Frederick H. Allen Endowed Chair in Child Psychiatry**

Holder: Tami D. Benton, MD

› **Gisela and Dennis Alter Endowed Chair in Pediatric Neonatology**

Holder: Haralambos Ischiropoulos, PhD

› **Mary D. Ames Endowed Chair in Child Advocacy**

Holder: David Rubin, MD, MSCE

› **Richard M. Armstrong Jr. Endowed Chair in Pediatric Orthopaedic Surgery**

Holder: John M. Flynn, MD

› **T. Hewson Bache Endowed Chair in Pediatrics**

Holder: Robert W. Doms, MD, PhD

› **Lester Baker Endowed Chair in Pediatric Diabetes**

Holder: Michael A. Levine, MD

› **Michael and Charles Barnett Endowed Chair in Pediatric Mitochondrial Medicine and Metabolic Diseases**

Holder: Douglas Wallace, PhD

› **James Battaglia Endowed Chair in Pediatric Pain Management**

Holder: Gordon Barr, PhD

› **William H. Bennett Professor of Pediatrics (at the University of Pennsylvania School of Medicine)**

Holder: Nathan Blum, MD

› **Fred and Suzanne Biesecker Endowed Chair in Pediatric Liver Disease**

Holder: David A. Piccoli, MD

› **Patricia Borns Endowed Chair in Radiology Education**

Holder: Janet R. Reid, MD

› **Irma and Norman Braman Endowed Chair for Research in GI Motility Disorders**

Holder: Robert O. Heuckeroth, MD, PhD

- › **Evelyn Willing Bromley Endowed Chair in Clinical Laboratories and Pathology**
Holder: Michael Bennett, PhD
- › **Evelyn Willing Bromley Endowed Chair in Pathology and Clinical Laboratories**
Holder: Nancy B. Spinner, PhD, FACMG
- › **Catherine D. Brown Endowed Chair in Pediatric Epilepsy**
Holder: Dennis Dlugos, MD
- › **Buck Family Endowed Chair in Hematology Research**
Holder: Pending Appointment
- › **Mortimer J. Buckley Jr., MD Endowed Chair in Cardiac Surgery**
Holder: Thomas L. Spray, MD
- › **Daniel B. Burke Endowed Chair for Diabetes Research**
Holder: Struan Grant, PhD
- › **Louis and Amelia Canuso Family Endowed Chair for Clinical Research in Oncology**
Holder: Frank M. Balis, MD
- › **Henry S. Cecil, MD Endowed Chair in Rehabilitative Medicine at Children's Seashore House**
Holder: Susan E. Levy, MD
- › **Children's Hospital of Philadelphia Endowed Chair in Anesthesiology and Critical Care Quality and Patient Safety**
Holder: Pending Appointment
- › **Children's Hospital of Philadelphia Endowed Chair in Biomedical Informatics and Entrepreneurial Science**
Holder: Fuchiang Tsui, PhD
- › **Children's Hospital of Philadelphia Endowed Chair in Cardiac Critical Care Medicine**
Holder: Andrew T. Costarino, MD
- › **Children's Hospital of Philadelphia Endowed Chair in Critical Care Medicine**
Holder: Vinay Nadkarni, MD
- › **Children's Hospital of Philadelphia Endowed Chair in Fetal Imaging**
Holder: Beverly Gilbert Coleman, MD
- › **Children's Hospital of Philadelphia Endowed Chair in Genomic Research**
Holder: Hakon Hakonarson, MD, PhD
- › **Children's Hospital of Philadelphia Endowed Chair in Pediatric Cardiothoracic Surgery**
Holder: Pending Appointment
- › **Children's Hospital of Philadelphia Endowed Chair in Pediatric Hematology**
Holder: Rodney Camire, PhD
- › **Children's Hospital of Philadelphia Endowed Chair in Pediatric Neuroradiology**
Holder: Giulio Zuccoli, MD
- › **Children's Hospital of Philadelphia Endowed Chair in Pediatric Orthopaedic Surgery**
Holder: Pending Appointment

- › **Children's Hospital of Philadelphia Endowed Chair in Pediatric Otolaryngology**
Holder: Ken Kazahaya, MD
- › **Children's Hospital of Philadelphia Endowed Chair in Pediatric Otolaryngology and Pediatric Airway Disorders**
Holder: Ian N. Jacobs, MD
- › **Alan R. Cohen Endowed Chair in Pediatrics**
Holder: Peter Adamson, MD
- › **Ruth M. Colket Endowed Chair in Pediatric Nursing**
Holder: Martha A. Q. Curley, RN, PhD, FAAN
- › **Ruth M. and Tristram C. Colket, Jr. Endowed Chair in Pediatric Surgery**
Holder: Alan W. Flake, MD
- › **Tristram C. Colket, Jr. Endowed Chair in Pediatric Neurology**
Holder: Robert R. Clancy, MD
- › **Colman Family Endowed Chair in Pediatric Inflammatory Bowel Disease**
Holder: Robert N. Baldassano, MD
- › **David Cornfeld Endowed Chair in Pediatrics**
Holder: Richard Rutstein, MD
- › **Jean Cortner Endowed Chair in Pediatric Gastroenterology**
Holder: Virginia A. Stallings, MD
- › **Nicholas Crognale Endowed Chair in Pediatric Emergency Medicine**
Holder: Kathy N. Shaw, MD
- › **Giulio D'Angio Endowed Chair in Neuroblastoma Research**
Holder: John Maris, MD
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Phillip Bryant, DO
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Susan Coffin, MD
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Diva D. De León-Crutchlow, MD, MSCE
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Angela M. Ellison, MD
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Alex Fiks, MD, MSCE
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Jeffrey S. Gerber, MD, PhD
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Ian Krantz, MD

- › **Distinguished Chair in the Department of Pediatrics**
Holder: Cynthia J. Mollen, MD
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Anne F. Reilly, MD, MPH
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Jonathan Rome, MD
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Maully J. Shah, MBBS
- › **Distinguished Chair in the Department of Pediatrics**
Holder: Flaura Winston, MD, PhD
- › **Distinguished Chair in the Department of Pediatrics**
Holders: Pending Appointment
- › **John J. Downes, MD Endowed Chair in Pediatric Anesthesiology and Critical Care Medicine**
Holder: C. Dean Kurth, MD
- › **Mary Downs Endowed Chair in Pediatric Craniofacial Treatment and Research**
Holder: Scott P. Bartlett, MD
- › **John W. Duckett, Jr. Endowed Chair in Pediatric Urology**
Holder: Stephen A. Zderic, MD
- › **Endowed Chair in Pediatric Interventional Radiology**
Holder: Anne Marie Cahill, MD
- › **Audrey E. Evans Endowed Chair in Pediatric Oncology**
Holder: Garrett M. Brodeur, MD
- › **Kenneth E. Fellows Endowed Chair in Radiology Quality and Patient Safety**
Holder: Raymond Sze, MD, MAMS
- › **Mark Fishman Endowed Chair in Genomics and Computational Science**
Holder: Joseph Zorc, MD, MSCE
- › **Richard and Ann Frankel Chair in Gastroenterology Research**
Holder: Pending Appointment
- › **Kwame Ohene-Frempong Endowed Chair in Pediatric Hematology**
Holder: Stefano Rivella, MD
- › **Friends of Brian Endowed Chair in Pediatric Plastic and Reconstructive Surgery**
Holder: Pending Appointment
- › **Lynne L. Garbose Endowed Chair in Fetal Family Care**
Holder: Lori J. Howell, DNP, MS, RN
- › **William T. Grant Endowed Chair in Child Development and Rehabilitation**
Holder: Marc Yudkoff, MD

- › **William J. Greeley Endowed Chair in Pediatric Anesthesiology and Critical Care Research**
Holder: Francis McGowan, MD
- › **Jane Fishman Grinberg Endowed Chair in Stem Cell Research**
Holder: Mortimer Poncz, MD
- › **Steven D. Handler Endowed Chair in Medical Ethics**
Holder: Christopher Feudtner, MD, PhD, MPH
- › **Robert and Dolores Harrington Endowed Chair in Pediatric Cardiology**
Holder: Jack Rychik, MD
- › **George Leib Harrison Endowed Chair in Fetal Therapy**
Holder: Julie S. Moldenhauer, MD
- › **Werner and Gertrude Henle Endowed Chair**
Holder: Theoklis Zaoutis, MD, MSCE
- › **Maurice R. Hilleman Endowed Chair in Vaccinology**
Holder: Paul Offit, MD
- › **Joseph Lee Hollander Endowed Chair in Pediatric Rheumatology**
Holder: Edward Behrens, MD
- › **John Westgate Hope Endowed Chair in Radiology Faculty Development**
Holder: Pending Appointment
- › **Justin Michael Ingerman Endowed Chair for Palliative Care**
Holder: Wynne Morrison, MD
- › **Orton P. Jackson Endowed Chair in Adolescent Medicine**
Holder: Carol Ford, MD
- › **John H. and Hortense Cassell Jensen Endowed Chair in Pediatric Development and Teaching**
Holder: Stephen Ludwig, MD
- › **Richard B. Johnston, Jr. Endowed Chair in Pediatrics**
Holder: Ronald Rubenstein, MD, PhD
- › **Joshua Kahan Endowed Chair in Pediatric Leukemia Research**
Holder: Carolyn Felix, MD
- › **Jacob A. Kamens Endowed Chair in Neurological Disorders and Translational NeuroTherapeutics**
Holder: Adeline Vanderver, MD
- › **John M. Keating Endowed Chair in Pediatrics**
Holder: Pending Appointment
- › **C. Everett Koop Endowed Chair in Pediatric Surgery**
Holder: N. Scott Adzick, MD
- › **Laffey-Connolly Endowed Chair in Pediatric Nephrology**
Holder: Susan Furth, MD

- › **Harriet and Ronald Lassin Endowed Chair in Pediatric Neonatology**
Holder: Scott Lorch, MD
- › **Anthony A. Latini Endowed Chair in the Prevention of Child Abuse and Neglect**
Holder: Cindy Christian, MD
- › **Elizabeth Paige Lavin Endowed Chair in Reserch in Clinical Care and Immunology**
Holder: Pending Appointment
- › **Dr. Bong S. Lee Endowed Chair in Pediatric Orthopaedics**
Holder: Maurizio Pacifici, PhD
- › **Mabel E. Leslie Endowed Chair in Pediatric Ophthalmology**
Holder: Monte D. Mills, MD
- › **Francis West Lewis Endowed Chair in Computational and Genomic Medicine**
Holder: Yi Xing, PhD
- › **Grace R. Loeb Endowed Chair in Neurosciences**
Holder: Brenda Banwell, MD
- › **Stephen Ludwig Endowed Chair in Medical Education**
Holder: Lisa Zaoutis, MD
- › **Suzi and Scott Lustgarten Endowed Chair for Clinical Care of GI Motility Disorders**
Holder: Ritu Verma, MBChB
- › **Soroosh Mahboubi Endowed Chair in Body Imaging at Children's Hospital of Philadelphia**
Holder: Pending Appointment
- › **Arthur Vincent Meigs Endowed Chair in Pediatrics**
Holder: Beverly Davidson, PhD
- › **Minimally Invasive Surgery Endowed Chair in Pediatric Urology**
Holder: Aseem R. Shukla, MD
- › **Jeffrey Modell Endowed Chair in Pediatric Immunology Research**
Holder: Neil Romberg, MD
- › **Robert Gerard Morse Endowed Chair in Pediatric Pulmonary Medicine**
Holder: Julian Allen, MD
- › **Thomas Moshang Endowed Chair in Endocrinology**
Holder: Craig Alter, MD
- › **E. Mortimer Newlin Endowed Chair in Pediatric Otolaryngology and Human Communication**
Holder: Ralph Wetmore, MD
- › **Edmond F. Notebaert Endowed Chair in Pediatric Research**
Holder: Bryan Wolf, MD, PhD
- › **Yetta Deitch Novotny Endowed Chair in Pediatric Oncology**
Holder: Stephan Grupp, MD, PhD

- › **Oberkircher Family Endowed Chair in Pediatric Radiology**
Holder: Timothy Roberts, PhD
- › **Patrick S. Pasquariello Jr. Endowed Chair in General Pediatrics**
Holder: Louis M. Bell, MD
- › **R.A.F. Penrose Endowed Chair in Pediatrics**
Holder: Stewart A. Anderson, MD
- › **Jeffrey E. Perelman Distinguished Chair in the Department of Pediatrics**
Holder: Stephen Hunger, MD
- › **Perelman Scholars**
Holders: Pending Appointment
- › **Raymond G. Perelman Endowed Chair in Pediatric Neuro-Ophthalmology**
Holder: Grant T. Liu, MD
- › **R. Anderson Pew Distinguished Chair in the Department of Pediatrics**
Holder: Kristy B. Arbogast, PhD
- › **Stanley Plotkin Endowed Chair in Pediatric Infectious Diseases**
Holder: Jeffrey M. Bergelson, MD
- › **William Potsic Endowed Chair in Pediatric Otolaryngology and Childhood Communication**
Holder: Pending Appointment
- › **Gerald D. Quill Distinguished Chair in the Department of Pediatrics**
Holder: Ron Keren, MD, MPH
- › **Peter Randall Endowed Chair in Plastic and Reconstructive Surgery**
Holder: Jesse A. Taylor, MD
- › **Russell C. Raphaely Endowed Chair in Critical Care Medicine**
Holder: Robert A. Berg, MD
- › **William J. Rashkind Endowed Chair in Pediatric Cardiology**
Holder: Robert J. Levy, MD
- › **Regional Autism Center Endowed Chair**
Holder: Robert T. Schultz, PhD
- › **Mildred L. Roeckle Endowed Chair at Children's Hospital of Philadelphia**
Holder: Andrei Thomas-Tikhonenko, PhD
- › **Lucy Balian Rorke-Adams Endowed Chair in Neuropathology**
Holder: Pending Appointment
- › **Richard and Sheila Sanford Endowed Chair in Pediatric Oncology**
Holder: Alex Seif, MD, MPH
- › **Louise Schnauffer Endowed Chair in Pediatric Surgery**
Holder: Holly L. Hedrick, MD

- › **Hubert J.P. and Anne Faulkner Schoemaker Endowed Chair in Pediatric Neuro-Oncology**
Holder: Michael Fisher, MD
- › **Elias Schwartz, MD Endowed Chair in Hematology**
Holder: Kim Smith-Whitley, MD
- › **Letitia B. and Alice Scott Endowed Chair in Human Genetics and Molecular Biology**
Holder: Elaine H. Zackai, MD
- › **Thomas Frederick McNair Scott Endowed Chair in Pediatrics**
Holder: Eric Eichenwald, MD
- › **Richard Shafritz Endowed Chair in Pediatric Ophthalmology Research in the Division of Ophthalmology**
Holder: Gil Binenbaum, MD, MSCE
- › **William Wikoff Smith Endowed Chair in Pediatric Genomic Research**
Holder: Fanxin Long, PhD
- › **Howard M. Snyder III Endowed Chair in Pediatric Urology**
Holder: Thomas F. Kolon, MD
- › **Louis Starr Endowed Chair in Pediatrics**
Holder: Pending Appointment
- › **Stuart E. Starr Endowed Chair in Pediatrics**
Holder: Jonathan Spergel, MD, PhD
- › **Surgical Technology and Technique Endowed Chair in Pediatric Surgery**
Holder: Thane A. Blinman, MD
- › **Leslie N. Sutton Endowed Chair in Pediatric Neurosurgery**
Holder: Phillip B. Storm Jr., MD
- › **Daniel M. Tabas Endowed Chair in Pediatric Cardiothoracic Surgery**
Holder: J. William Gaynor, MD
- › **Evelyn Rome Tabas Endowed Chair in Pediatric Cardiology**
Holder: Victoria L. Vetter, MD
- › **Josephine J. Templeton Endowed Chair in Pediatric Anesthesiology Clinical Education**
Holder: Susan C. Nicolson, MD
- › **Josephine J. and John M. Templeton Jr. Endowed Chair in Pediatric Trauma**
Holder: Michael L. Nance, MD, FAAP, FACS
- › **Jennifer Terker Endowed Chair in Pediatric Cardiology**
Holder: Joseph Rossano, MD
- › **Charles E.H. Upham Endowed Chair in Pediatric Medicine**
Holder: Beverly S. Emanuel, PhD
- › **William L. Van Alen Endowed Chair in Pediatric Radiology**
Holder: Kassa Darge, MD, PhD

- › **Frank R. Wallace Endowed Chair in Infectious Diseases**
Holder: Kathleen Sullivan, MD, PhD
- › **Alice Langdon Warner Endowed Chair in Pediatric Cardiothoracic Surgery**
Holder: Christopher E. Mascio, MD
- › **Wawa Endowed Chair in International Adoption**
Holder: Susan Friedman, MD
- › **Frank E. Weise III Endowed Chair in Pediatric Hematology**
Holder: Gerd Blobel, MD, PhD
- › **Mai and Harry F. West Endowed Chair in Pediatric Research**
Holder: Pending Appointment
- › **Alexander B. Wheeler Endowed Chair in Neurosurgical Research**
Holder: Adam Resnick, PhD
- › **Evelyn and George Willing Endowed Chair in Pathology Research**
Holder: Janis Burkhardt, PhD
- › **Nancy Abramson Wolfson Endowed Chair in Health Services Research**
Holder: Jeffrey H. Silber, MD, PhD
- › **Richard D. Wood Jr. and Jeanette A. Wood Endowed Chair in Pediatric Diagnostic Medicine**
Holder: Pending Appointment

ADMINISTRATIVE UNITS

- › **Clinical Research Support Office**
Michele Toms, RN, Administrative Director, Staffing Core
- › **Clinical Trials Financial Management**
Veronica Kain, Director
- › **Core Facilities Administration**
Lisa MacDowell, Director
- › **Faculty Development**
Mary Blitzer Field, PhD, Assistant Director
- › **Research Communications**
Jennifer Long, Director
- › **Research Compliance and Regulatory Affairs**
Matthew Hodgson, Assistant Vice President
- › **Research Finance**
Steven Wiley, Senior Director
Luz Arrison, Assistant Director
Bethann Kurek, Assistant Director
- › **Research Information Systems**
Michael Schultz, Director

› **Research Resources**

Howard Eck, Director

› **Research Safety**

Denise Melvin, Director

› **Sponsored Projects and Research Business Management**

Sara Dubberly, Director

Brigid Czystczyn, Assistant Director

Robert Denight, Assistant Director

› **Office of Technology Transfer, Innovation and Research Contracts**

Zev Sunleaf, Vice President Thomas Privette, PhD, Office of Entrepreneurship and Innovation

Camille Jolly-Tornetta, Office of Collaborative and Corporate Research Contracts

› **Department of Veterinary Resources**

Laike Stewart, DVM, DACLAM, Attending Veterinarian

› **Research Compliance and Regulatory Affairs**

Matthew Hodgson, Assistant Vice President



CREDITS

- › **Madeline Bell**
Chief Executive Officer
- › **Bryan A. Wolf, MD, PhD**
Chief Scientific Officer & Executive Vice President
- › **Michelle A. Lewis**
Vice President, Research Administration and Operations
- › **Jennifer Long**
Director, Research Communications
- › **Sharlene George**
Senior Medical/Science Writer
- › **Jillian Lim**
Medical/Science Writer
- › **Barbara Drosey**
Medical/Science Writer
- › **Nancy McCann**
Medical/Science Writer
- › **Angela Knott**
Art Director
- › **Juliet Kilcoyne**
Creative Designer & Developer
- › **Melissa LaVigne**
Graphic Designer
- › **Alexis Arvanitides**
Graphic Designer



LINKS OF INTEREST

- › [Children's Hospital of Philadelphia Research Institute Website](#)
- › [Cornerstone](#), CHOP Research Institute's blog
- › [CHOP Research Institute Press Releases](#)
- › [Bench to Bedside](#), CHOP Research's Monthly Online Newsmagazine
- › CHOP Research Institute's [Facebook Page](#)
- › CHOP Research Institute's [Twitter Feed](#)
- › CHOP Research Institute's [LinkedIn Page](#)
- › CHOP Research Institute's [Instagram Page](#)
- › CHOP Research Institute's [YouTube Channel](#)
- › [Children's Hospital of Philadelphia Website](#)
- › Children's Hospital of Philadelphia [YouTube Channel](#)
- › [Children's Hospital of Philadelphia Foundation Website](#)

CHOP Research Institute's Department of Research Communications produced the 2018 Research Annual Report.

© 2018 by Children's Hospital of Philadelphia Research Institute. All Rights Reserved.